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(71) Applicant (*for all designated States except US*): G.D. SEARLE & CO. [US/US]; Corporate Patent Department, 5200 Old Orchard Road, Skokie, IL 60077 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): TOLLEFSON, Michael, B. [US/US]; 357 Big Horn Drive, Hainesville, IL 60030 (US). KOLODZIEJ, Steve, A. [US/US]; 2448 Clinton Road, Ballwin, MO 63021 (US). REITZ, David, B. [US/US]; 14814 Pleasant Ridge Court, Chesterfield, MO 63017 (US).

(74) Agents: WARNER, James, M. et al.; G.D. Searle & Co., Corporate Patent Department, 5200 Old Orchard Road, Skokie, IL 60077 (US).

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(57) Abstract

Novel 1,2-benzothiazepines, derivatives and analogs thereof, pharmaceutical compositions containing them, and their use in medicine, particularly in the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders, such as those associated with atherosclerosis and/or hypercholesterolemia.

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NOVEL 1,2-BENZOTHIAZEPINES HAVING ACTIVITY AS INHIBITORS OF ILEAL BILE ACID TRANSPORT AND TAUROCHOLATE UPTAKE

Field of the Invention

The present invention relates to novel 1,2-benzothiazepines, derivatives and analogs thereof, pharmaceutical compositions containing them, and their use in medicine, particularly in the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders, such as those associated with atherosclerosis and/or hypercholesterolemia, in mammals.

Description of Related Art

It is well-settled that hyperlipidemic conditions associated with elevated concentrations of total cholesterol and low-density lipoprotein ("LDL") cholesterol are major risk factors for coronary heart disease and particularly atherosclerosis. Interfering with the circulation of bile acids within the lumen of the intestinal tract is found to reduce the levels of serum cholesterol in a causal relationship. Epidemiological data has accumulated which indicates such reduction leads to an improvement in the disease state of atherosclerosis. Stedronsky, "Interaction Of Bile Acids And Cholesterol With Nonsystemic Agents Having Hypocholesterolemic Properties," Biochimica et Biophysica Acta, 1210 (1994) 255-287, discusses the biochemistry, physiology and known active agents relating to bile acids and cholesterol.

Pathophysiologic alterations are shown to be consistent with interruption of the enterohepatic circulation of bile acids in humans in Heubi, J.E., et al., "Primary Bile Acid Malabsorption: Defective *In Vitro* Ileal Active Bile Acid Transport", Gastroenterology, 1982:83:804-11.

In fact, cholestyramine binds the bile acids in the intestinal tract, thereby interfering with their normal enterohepatic circulation. Reihnér, E. et al, in "Regulation of Hepatic Cholesterol Metabolism In Humans: Stimulatory Effects Of Cholestyramine On HMG-CoA Reductase Activity And Low Density Lipoprotein Receptor Expression In Gallstone Patients", Journal of Lipid Research, Volume 31, 1990, 2219-2226. This results in an increase in liver bile acid synthesis by the liver using cholesterol as well as an upregulation of the liver LDL receptors which enhances clearance of cholesterol and decreases serum LDL cholesterol levels. Suckling el al, "Cholesterol Lowering And Bile Acid Excretion In The Hamster With Cholestyramine Treatment", Atherosclerosis, 89(1991) 183-190), also discloses the results of cholestyramine treatment to lower serum cholesterol levels.

In another approach to the reduction of recirculation of bile acids, the ileal bile acid transport system is a putative pharmaceutical target for the treatment of hypercholesterolemia based on an interruption of the enterohepatic circulation with specific transport inhibitors. Kramer, et al, "Intestinal Bile Acid Absorption", The Journal of Biological Chemistry, Vol. 268, No. 24, Issue of August 25, pp. 18035-18046, 1993.

In a series of patent applications, Hoechst Aktiengesellschaft discloses polymers of various naturally occurring constituents of the enterohepatic circulation system and their derivatives, including bile acid, which inhibit the physiological bile acid transport with the goal of reducing the LDL cholesterol level sufficiently to be effective as pharmaceuticals and, in particular for use as hypocholesterolemic agents. See, e.g., Canadian Patent Application Nos. 2,025,294; 2,078,588; 2,085,782; and 2,085,830; and EP Application Nos. 0 379 161; 0 549 967; 0 559 064; and 0 563 731.

In vitro bile acid transport inhibition is disclosed to show hypolipidemic activity in The Wellcome Foundation Limited disclosure of the

world patent application number WO 93/16055 for "Hypolipidemic Benzothiepine Compounds".

Selected benzothiepines are disclosed in world patent application number WO93/321146 for numerous uses including fatty acid metabolism and coronary vascular diseases.

Additional benzothiepines for use as hypolipidemic agents are disclosed in WO97/33882 and U.S. Patent 5,994,391.

Other selected benzothiepines are known for use as hypolipaemic and hypocholesterolaemic agents, especially for the treatment or prevention of atherosclerosis as disclosed by application Nos. EP 508425, FR 2661676, and WO 92/18462, each of which is limited by an amide bonded to the carbon adjacent the phenyl ring of the fused bicyclo benzothiepine ring.

WO96/16051 published May 30, 1996 describes certain 1,5-benzothiazepines as useful in the treatment of hyperlipidemic conditions.

WO96/05188 published February 22, 1996 describes certain 1,4-benzothiazepines as useful in the treatment of hyperlipidemic conditions.

Additional benzothiazepines are discussed in the references set forth below. These references either do not disclose a specific utility or disclose a different utility than the present invention.

Orahovats et al., "A Ring Enlargement From Seven- To Ten-Membered-Ring Sulfonamide Derivatives", Helv. Chim. Acta, vol. 79, pp. 1121-1128 (1996) describes 4,5-dihydro-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide.

Katrizky et al., "Preparation Of 6-, 7- and 8-Membered Sultams By Friedel-Crafts Cyclization Of ω-Phenylalkanesulfamoyl Chlorides", Org. Prep. Proced. Int., vol. 24(4), pp. 463-467 (1992) describes 2,3,4,5-tetrahydro-1,2-benzothiazepine-1,1-dioxide and 2,3,4,5-tetrahydro-2-butyl-1,2-benzothiazepine-1,1-dioxide for possible use as an anticonvulsant, diuretic or sedative.

Beckwith et al., "Iododediazoniation Of Arenediazonium Salts Accompanied By Aryl Radical Ring Closure", J. Org. Chem., vol. 52, pp. 1922-1930 (1987) describes 2,3,4,5-tetrahydro-2-allyl-1,2-benzothiazepine-1,1-dioxide.

Stassinopolou et al., "^{13}C NMR Spectra Of Benzothiazepine, Benzothiazone and Benzosulphonamide N-substituted Derivatives", Org. Magn. Reson., vol. 21(3), pp. 187-189 (1983), describes certain N-substituted 4,5-dihydro-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxides.

Tamura et al., "Novel Conversions Of Benzo[b]thiophen-3(2H)-ones Into 1,2-Benzisothiazole And Tetrahydro-1,2-benzothiazepin-5-One Systems Via Sulphimide Intermediates", J. Chem. Soc., Perkin Trans. I, vol. 12, pp. 2830-2834 (1980) describes 2,3,4,5-tetrahydro-2-tosyl-4-methyl-1,2-benzothiazepine-5-one-1,1-dioxide.

Catsoulacos et al., "Synthesis Of Some N-Substituted 4,5-Dihydro-7,8-dimethoxybenzothiazepin-3-one 1,1-Dioxides, J. Hetero. Chem., vol. 13(6), pp. 1309-1314 (1976) describes 4,5-dihydro-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide and certain 4,5-dihydro-2-(phenyl, substituted phenyl or pyridyl)-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxides having anti-inflammatory and central nervous system activity.

Pangiotopoulos et al., "N(p-Bromophenyl)-4,5-Dihydro-7,8-Dimethoxy Benzothiazepine-3-One 1,1-Dioxide $C_{17}H_{16}BrNO_4S$", Cryst. Struct. Comm., vol. 9, pp. 313-320 (1980) describes 4,5-dihydro-2-(4-bromo-phenyl)-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide.

Catsoulacos et al., "Thiazo Compounds: Derivatives Of 4,5-Dihydro-7,8-Dimethoxybenzothiazepin-3-one 11-Dioxides", J. Chem. Eng. Data, vol. 22(3), pp. 353-354 (1977) describes 4,5-dihydro-2-(ethyl, n-propyl or isopropyl)-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxide.

Camoutsis et al., "N-Substituted 4,5-Dihydro-1,2-benzothiaepin-3-one 1,1-Dioxide", J. Hetero. Chem., vol. 17(5), pp. 1135-1136 (1980) describes

certain 4,5-dihydro-2-(3- or 5-pyridyl)-7,8-dimethoxy-1,2-benzothiazepine-3-one-1,1-dioxides.

U.S. Patent No. 5,350,761 describes hydroxylamine derivatives that generically encompass certain benzothiazepine compounds. These derivatives are described as lipoxygenase inhibitors useful in the treatment of inflammatory and allergic conditions.

WO98/02432 published January 22, 1998 describes certain 5-(aryl-(N-containing-heterocyclyl)alkyl)benzothiazepines and aralkyl-(N-containing-heterocyclyl)alkyl)-benzothiazepines as useful for controlling micturition.

WO97/03953 published February 6, 1997 describes certain sulfonylamino-substituted benzothiazepines as inhibitors of the enzyme cyclooxygenase II.

WO95/21843 published August 17, 1995 describes certain benzothiazepines substituted with azacyclic condensed piperazines. These compounds are identified as kappa receptor agonists useful as analgesics and diuretics and for the treatment of cerebral ischaemia.

EP338331 published October 25, 1989 describes certain 2-benzothiazepine-5-ones useful as muscle relaxants.

Summary of the Invention

A first aspect of the invention comprises novel 1,2- benzothiazepines that are effective agents for the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders.

A second aspect of the invention comprises pharmaceutical compositions comprising the novel 1,2- benzothiazepines that are suitable for the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders.

A third aspect of the invention comprises methods for the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders

comprising administering to a subject a prophylactically or therapeutically effective amount of one of the novel 1,2- benzothiazepines.

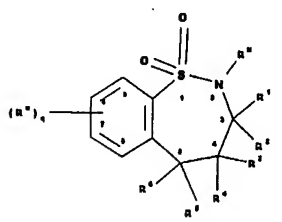
A fourth aspect of the invention comprises methods of making the novel 1,2-benzothiazepines of the present invention.

Additional aspects of the invention are discussed throughout the specification of this application.

Detailed Description of the Invention

The following detailed description is provided to aid those skilled in the art in practicing the present invention. This detailed description, however, should not be construed to unduly limit the present invention as modifications and variations in the embodiments discussed herein can be made by those of ordinary skill in the art without departing from the spirit or scope of the present inventive discovery. The contents of each of the references cited herein, including the contents of the references cited within these primary references, are herein incorporated by reference in their entirety.

Accordingly, the present invention provides compounds corresponding to the structure of Formula (I):



(I)

wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

R^3 and R^4 are independently selected from the group consisting of hydrogen; hydrocarbyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form $=O$; $=NOR^9$; $=S$; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^9 and R^{10} are independently selected from the group consisting of hydrogen; hydrocarbyl; amino; and hydrocarbylamino; wherein said hydrocarbyl moieties may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl moieties optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; hydrocarbyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

R^5 and R^6 are independently selected from the group consisting of

hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; $-NO_2$; -CN; oxo; hydrocarbyl; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; $-OM$; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein A^- is a pharmaceutically acceptable anion, and M is a

pharmaceutically acceptable cation; and

wherein R^9 is as defined above; or

R^4 and R^6 together represent a bond; and

R^N is selected from the group consisting of hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

one or more R^X radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; hydrocarbyl; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-S(O)_2R^{13}$; $-SO_3R^{13}$; $-S^+R^{13}R^{14}A^-$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-NR^{14}C(O)R^{13}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-S(O)_nNR^{13}R^{14}$; $-N^+R^{13}R^{14}R^{15}A^-$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

wherein n is 0, 1 or 2; and

wherein R^{13}, R^{14}, R^{15}, A^-, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

provided that at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is a radical other than hydrogen or alkyl; and

provided that when R^5 or R^6 is aryl, the other of R^5 and R^6 is a radical other than heterocycylalkyl.

A preferred class of compounds comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl;

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^wA^-$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P(O)R^9$-; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl;

heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; carboxyalkylamino; alkoxyalkylamino; and acyl; or

wherein A^- is a pharmaceutically acceptable anion; and

R^3 and R^4 are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form $=O$; $=NOR^9$; $=S$; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cyanoalkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

R^5 and R^6 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^3 and R^4 radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A$-; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may have one or more carbons replaced by -O-; $-NR^7$-; $-N^+R^7R^8A^-$; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$; $-PR^7$-; $-P(O)R^7$-; $-P^+R^7R^8A^-$; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-P^{9}R^{10}$; $-P^{+}R^{9}R^{10}R^{11}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^{9}-$; $-N^{+}R^{9}R^{10}A^{-}-$; -S-; -SO-; $-SO_2-$; $-S^{+}R^{9}A^{-}-$; $-PR^{9}-$; $-P^{+}R^{9}R^{10}A^{-}-$; $-P(O)R^{9}-$; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group

consisting of R^{9} and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{w}, and A^{-} are as defined above; and

R^{N} is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aralkyl; and heterocyclylalkyl; and

one or more R^{X} radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-S(O)_2R^{13}$; $-SO_3R^{13}$; $-S^{+}R^{13}R^{14}A^{-}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-NR^{14}C(O)R^{13}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-OR^{18}$; $-S(O)_nNR^{13}R^{14}$; $-NR^{13}R^{18}$; $-NR^{18}OR^{14}$; $-N^{+}R^{13}R^{14}R^{15}A^{-}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue;

wherein the R^{x} alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-P^{9}R^{10}$; $-P^{+}R^{9}R^{11}R^{12}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

wherein the R^{x} quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; -

$P(O)R^{13}R^{14}$; $-P^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; $-P(OR^{13})OR^{14}$; $-S^{+}R^{13}R^{14}A^{-}$; $-N^{+}R^{13}R^{14}R^{15}A^{-}$; and carbohydrate residue; and

wherein the R^{x} radicals comprising carbon optionally may have one or more carbons replaced by -O-; $-NR^{13}$-; $-N^{+}R^{13}R^{14}A^{-}$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{13}A^{-}$-; $-PR^{13}$-; $-P(O)R^{13}$-; $-PR^{13}R^{14}$; $-P^{+}R^{13}R^{14}A^{-}$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; $-NR^{9}$-; $-N^{+}R^{9}R^{10}A^{-}$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{9}A^{-}$-; $-PR^{9}$-; $-P^{+}R^{9}R^{10}A^{-}$-; or $-P(O)R^{9}$-; and

wherein R^{18} is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R^{18} alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN ; NO_2; oxo; $-OR^{9}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{11}R^{12}A^{-}$; $-SR^{9}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{9}$; $-CO_2R^{9}$; $-CONR^{9}R^{10}$; $-SO_2OM$; $-SO_2NR^{9}R^{10}$; $-PR^{9}R^{10}$; $-P(OR^{13})OR^{14}$; $-PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{w}, A^{-}, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

In the various embodiments of the invention, R^{5} and R^{6} preferably are independently selected from the group consisting of H; aryl;

heterocyclyl; and quaternary heterocyclyl;

wherein the R^{5} and R^{6} aryl; heterocyclyl; and quaternary heterocyclyl; radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; -C(O)NR^{13}R^{14}; -C(O)OM; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; $-P(OR^{13})OR^{14}$; $-S^{+}R^{13}R^{14}A^{-}$; and $-N^{+}R^{13}R^{14}R^{15}A^{-}$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^{5} and R^{6} radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^{7}$; $-NR^{7}R^{8}$; $-SR^{7}$; $-S(O)R^{7}$; $-SO_2R^{7}$; $-SO_3R^{7}$; $-CO_2R^{7}$; $-CONR^{7}R^{8}$; $-N^{+}R^{7}R^{8}R^{9}A$-; $-P(O)R^{7}R^{8}$; $-PR^{7}R^{8}$; $-P^{+}R^{7}R^{8}R^{9}A^{-}$; and $-P(O)(OR^{7})OR^{8}$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^{5} and R^{6} radicals optionally may have one or more carbons replaced by -O-; $-NR^{7}$-; $-N^{+}R^{7}R^{8}A$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{7}A$-; $-PR^{7}$-; $-P(O)R^{7}$-; $-P^{+}R^{7}R^{8}A$-; or phenylene; and

wherein R^{7} and R^{8} are independently selected from the group

consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^{9}R^{10}$; $-P^{+}R^{9}R^{10}R^{11}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl;

alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^{9}$-; $-N^{+}R^{9}R^{10}A^{-}$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{9}A^{-}$-; $-PR^{9}$-; $-P^{+}R^{9}R^{10}A^{-}$-; $-P(O)R^{9}$-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^{9} and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{w}, and A^{-} are as previously set forth above for the compounds of Formula I.

More preferably, R^{5} or R^{6} has the formula $-Ar-(R_y)_t$

wherein:

t is an integer from 0 to 5;

Ar is selected from the group consisting of phenyl; thiophenyl; pyridyl; piperazinyl; piperonyl; pyrrolyl; naphthyl; furanyl; anthracenyl; quinolinyl; isoquinolinyl; quinoxalinyl; imidazolyl; pyrazolyl; oxazolyl; isoxazolyl; pyrimidinyl; thiazolyl; triazolyl; isothiazolyl; indolyl; benzoimidazolyl; benzoxazolyl; benzothiazolyl; and benzoisothiazolyl; and

one or more R^{y} are independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; -

$P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y radicals optionally may have one or more carbons replaced by -O-; $-NR^7-$; $-N^+R^7R^8A^-$-; -S-; -SO-; $-SO_2-$; $-S^+R^7A^-$-; $-PR^7-$; $-P(O)R^7-$; $-P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they

are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

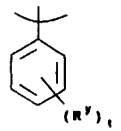
wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$-; $-PR^9-$; $-P^+R^9R^{10}A^-$-; $-P(O)R^9-$; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as previously set forth above for the compounds of Formula I.

Still more preferably, at least one of R^3 or R^4 has the formula (II)



(II)

wherein R^y and t are defined as above.

In the various embodiments of the invention, the compounds of Formula I preferably satisfy at least one or more of the following additional conditions:

(1) R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl and (C_{3-10})cycloalkyl. Preferably, R^1 and R^2 are independently selected from the group consisting of hydrogen and (C_{1-10})alkyl. More preferably, R^1 and R^2 are independently selected from the group consisting of (C_{1-10})alkyl. Still more preferably, R^1 and R^2 are independently selected from the group consisting of (C_{1-7})alkyl. Still more preferably, R^1 and R^2 are independently selected from the group consisting of (C_{2-4})alkyl. Still more preferably, R^1 and R^2 are the same (C_{2-4})alkyl. Still more preferably, R^1 and R^2 are each n-butyl; and/or

(2) R^3 and R^4 are independently selected from the group consisting of hydrogen and $-OR^9$ wherein R^9 is defined as previously set forth above for the compounds of Formula I. Preferably, R^3 is hydrogen and R^4 is $-OR^9$. Still more preferably, R^3 is hydrogen and R^4 is hydroxy. Still more preferably, the hydroxy group is in a syn relationship to the structure of Formula II; and/or

(3) R^5 is phenyl substituted with a radical selected from the group

consisting of $-OR^{13}$, $-NR^{13}R^{14}$, $-NR^{13}C(O)R^{14}$, $-NR^{13}C(O)NR^{14}R^{15}$, $-NR^{13}CO_2R^{14}$, $-OC(O)R^{13}$, $-OC(O)NR^{13}R^{14}$, $-NR^{13}SOR^{14}$, $-NR^{13}SO_2R^{14}$, $-NR^{13}SONR^{14}R^{15}$, and $-NR^{13}SO_2NR^{14}R^{15}$ wherein R^{13}, R^{14} and R^{15} are as previously set forth above for the compounds of Formula I. Still more preferably, R^5 is phenyl substituted with $-OR^{13}$ or $-NR^{13}C(O)R^{14}$. Still more preferably, R^5 is phenyl substituted at the para or meta position with $-OR^{13}$ wherein R^{13} comprises a quaternary heterocyclyl, quaternary heterocyclylalkyl or alkylammoniumalkyl, or R^5 is phenyl substituted at the para or meta position with $-NR^{13}C(O)R^{14}$ wherein R^{13} is hydrogen and R^{14} comprises a quaternary heterocyclyl, quaternary heterocyclylalkyl or alkylammoniumalkyl; and/or

(4) R^6 is hydrogen; and/or

(5) R^N is selected from the group consisting of hydrogen, alkyl and aralkyl. Preferably, R^N is selected from the group consisting of hydrogen, (C_{1-10})alkyl and aryl(C_{1-10})alkyl. More preferably, R^N is selected from the group consisting of hydrogen, methyl, ethyl and benzyl. Still more preferably, R^N is hydrogen; and/or

(6) R^x is independently selected from the group consisting of $-OR^{13}$, $-NR^{13}R^{14}$, $-N^+R^{13}R^{14}R^{15}A^-$, and polyether. More preferably, R^x is selected from the group consisting of $-OR^{13}$ and $-NR^{13}R^{14}$. Still more preferably, R^X is selected from the group consisting of alkoxy, amino, alkylamino and dialkylamino. Still more preferably, R^X is selected from the group consisting of methoxy and dimethylamino; and/or

(7) One or more R^x are present at the 7-, 8- or 9-position of the benzo ring of the structure of Formula I. Preferably, said R^x are present at the 7- and 9-positions of the benzo ring of the structure of Formula I. More preferably, R^x is present at the 7-position of the benzo ring of the structure of Formula I; and/or

(8) q is 1, 2 or 3. Preferably, q is 1 or 2, and more preferably q is 1;

and/or

(9) t is 1 or 2.

In still another embodiment of the invention, the compounds of Formula I satisfy at least one or more of the above-described conditions and R^5 comprises a carbohydrate residue.

A more preferred class of compounds comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl; and

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^w A^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^wA^-$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9$-; $-N^+R^9R^{10}A^-$; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P(O)R^9$-; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^w are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl;

carboxyalkyl; carboalkoxyalkyl; carboxyheterocyclyl; carboxyalkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3 and R^4 are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; carboxyalkyl; carboalkoxyalkyl; cycloalkyl; cyanoalkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

R^5 and R^6 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; -

$NR^{13}SO_2NR^{14}R^{15}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A$-; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may have one or more carbons replaced by -O-; $-NR^7$-; $-N^+R^7R^8A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$-; $-PR^7$-; $-P(O)R^7$-; $-P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen and alkyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; sulfoalkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9$-; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P^+R^9R^{10}A^-$-; $-P(O)R^9$-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as defined above; and

R^N is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; and aralkyl; and

one or more R^X radicals are independently selected from the group consisting of hydrogen; halogen; -CN; -NO_2; alkyl; cycloalkyl; polyalkyl; haloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; polyether; acyloxy; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -$S(O)R^{13}$; -$S(O)_2R^{13}$; -SO_3R^{13}; -$S^+R^{13}R^{14}A^-$; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$NR^{14}C(O)R^{13}$; -$C(O)NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -OR^{18}; -$S(O)_nNR^{13}R^{14}$; -$NR^{13}R^{18}$; -$NR^{18}OR^{14}$; -$N^+R^{13}R^{14}R^{15}A^-$; -$PR^{13}R^{14}$; -$P(O)R^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide acid residue; polypeptide acid residue; and carbohydrate acid residue;

wherein the R^x alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^wA^-$; -SR^{16}; -$S(O)R^9$; -SO_2R^9; -SO_3R^{16}; -CO_2R^{16}; -$CONR^9R^{10}$; -$SO_2NR^9R^{10}$; -$PO(OR^{16})OR^{17}$; -PR^9R^{10}; -$P^+R^9R^{11}R^{12}A^-$; -$S^+R^9R^{10}A^-$; and carbohydrate acid residue; and

wherein the R^x quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; -NO_2; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -$S(O)R^{13}$; -SO_2R^{13}; -SO_3R^{13}; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$C(O)NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -$P(O)R^{13}R^{14}$; -$PR^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; -$P(OR^{13})OR^{14}$; -$S^+R^{13}R^{14}A^-$; -$N^+R^{13}R^{14}R^{15}A^-$; and carbohydrate acid residue; and

wherein the R^X radicals comprising carbon optionally may have one or more carbons replaced by -O-; -NR^{13}-; -$N^+R^{13}R^{14}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^{13}A^-$-; -PR^{13}-; -$P(O)R^{13}$-; -PR^{13}-; -$P^+R^{13}R^{14}A^-$-; phenylene; amino

acid; peptide; polypeptide; carbohydrate; polyether; or polyalkyl; wherein said phenylene; amino acid; peptide; polypeptide; carbohydrate; and polyalkyl optionally may have one or more carbons replaced by -O-; -NR^9-; -$N^+R^9R^{10}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^9A^-$-; -PR^9-; -$P^+R^9R^{10}A^-$-; or -$P(O)R^9$-; and

wherein R^{18} is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R^{18} alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN ; oxo; -OR^9; -NR^9R^{10}; -$N^+R^9R^{11}R^{12}A^-$; -SR^9; -$S(O)R^9$; -SO_2R^9; -SO_3R^9; -CO_2R^9; -$CONR^9R^{10}$; -SO_2OM; -$SO_2NR^9R^{10}$; -PR^9R^{10}; -$P(OR^{13})OR^{14}$; -$PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^w, A^-, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

A class of compounds of interest comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkenyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkynyl; (C_1-C_{10})alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form (C_3-C_{10})cycloalkyl; and

wherein the R^1 and R^2 (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkenyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkynyl; (C_1-C_{10})alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^wA^-$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1 and R^2 (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkenyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkynyl; (C_1-C_{10})alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$-; $-PR^9$; $-P(O)R^9-$; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3 and R^4 are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group

consisting of hydrogen; -CN; halogen; oxo; (C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; cyano(C_1-C_{10})alkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

R^5 and R^6 are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; (C_1-C_{10})alkyl; polyalkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the (C_1-C_{10})alkyl, polyalkyl, halo(C_1-C_{10})alkyl, hydroxy(C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, aryl(C_1-C_{10})alkyl, heterocyclyl(C_1-C_{10})alkyl, and polyether substituents of the R^5 and R^6 radicals optionally

may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the (C_1-C_{10})alkyl, polyalkyl, halo(C_1-C_{10})alkyl, hydroxy(C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, aryl(C_1-C_{10})alkyl, heterocyclyl(C_1-C_{10})alkyl, and polyether substituents of the R^5 and R^6 radicals optionally may have one or more carbons replaced by -O-; $-NR^7$-; $-N^+R^7R^8A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$-; $-PR^7$-; $-P(O)R^7$-; $-P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen and (C_1-C_{10})alkyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaryl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaryl (C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aminocarbonyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkylaminocarbonyl (C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; (C_1-C_{10})alkyl; sulfo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; - $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaryl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aminocarbonyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9$-; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P^+R^9R^{10}A^-$-; $-P(O)R^9$-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as defined above; and

R^N is selected from the group consisting of hydrogen; (C_1-C_{10})alkyl;

(C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; and aryl(C_1-C_{10})alkyl; and

one or more R^X radicals are independently selected from the group consisting of hydrogen; halogen; -CN; -NO_2; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; halo(C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; polyether; acyloxy; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -$S(O)R^{13}$; -$S(O)_2R^{13}$; -SO_3R^{13}; -$S^+R^{13}R^{14}A^-$; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$NR^{14}C(O)R^{13}$; -$C(O)NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -OR^{18}; -$S(O)_nNR^{13}R^{14}$; -$NR^{13}R^{18}$; -$NR^{18}OR^{14}$; -$N^+R^{13}R^{14}R^{15}A^-$; -$PR^{13}R^{14}$; -$P(O)R^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide acid residue; polypeptide acid residue; and carbohydrate acid residue;

wherein the R^x (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; halo(C_1-C_{10})alkyl; hydroxy(C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; acyloxy radicals optionally may be further substituted with halogen; -CN; oxo; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{11}R^{12}A^-$; -SR^{16}; -$S(O)R^9$; -SO_2R^9; -SO_3R^{16}; -CO_2R^{16}; -$CONR^9R^{10}$; -$SO_2NR^9R^{10}$; -$PO(OR^{16})OR^{17}$; -PR^9R^{10}; -$P^+R^9R^{11}R^{12}A^-$; or -$S^+R^9R^{10}A^-$; and

wherein the R^x quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; -NO_2; oxo; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; halo(C_1-C_{10})alkyl; hydroxy(C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -$S(O)R^{13}$; -SO_2R^{13}; -SO_3R^{13}; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$C(O)NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -$P(O)R^{13}R^{14}$; -$PR^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; -$P(OR^{13})OR^{14}$; -$S^+R^{13}R^{14}A^-$; and -$N^+R^{13}R^{14}R^{15}A^-$; and

wherein the R^X radicals comprising carbon optionally may have one or more carbons replaced by -O-; -NR^{13}-; -$N^+R^{13}R^{14}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^{13}A^-$-; -PR^{13}-; -$P(O)R^{13}$-; -PR^{13}-; -$P^+R^{13}R^{14}A^-$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; -NR^9-; -$N^+R^9R^{10}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^9A^-$-; -PR^9-; -$P^+R^9R^{10}A^-$-; or -$P(O)R^9$-; and

wherein R^{18} is selected from the group consisting of (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; acyl; and aryl(C_1-C_{10})alkoxycarbonyl; and

wherein the R^{18} (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; acyl; and aryl(C_1-C_{10})alkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN ; oxo; -OR^9; -NR^9R^{10}; -$N^+R^9R^{11}R^{12}A^-$; -SR^9; -$S(O)R^9$; -SO_2R^9; -SO_3R^9; -CO_2R^9; -$CONR^9R^{10}$; -SO_2OM; -$SO_2NR^9R^{10}$; -PR^9R^{10}; -$P(OR^{13})OR^{14}$; -$PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^w, A^-, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

provided that aryl is selected from the group consisting of optionally substituted phenyl, biphenyl and naphthyl; and

provided that heterocyclyl is selected from the group consisting of optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.

A class of compounds of particular interest comprises those

compounds of Formula I wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, hexyl, phenoxymethylene, phenoxyethylene, phenoxypropylene, pyridinyloxymethylene, pyridinyloxyethylene; methylpyridinyloxymethylene, methylpyridinyloxyethylene, pyrimidinyloxymethylene, and pyrimidinyloxyethylene; or

R^1 and R^2 taken together with the carbon to which they are attached form cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl; and

R^3 and R^4 are independently selected from the group consisting of hydrogen, hydroxy, methyl, ethyl, phenyl, pyridinyl, amino, methylamino, dimethylamino, ethylamino and diethylamino; and

R^5 and R^6 are independently selected from the group consisting of hydrogen, phenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, hydroxyphenyl, methoxyphenyl, ethoxyphenyl, methoxy(chlorophenyl), methoxy(fluorophenyl), methoxy(bromophenyl), methoxy(iodophenyl), ethoxy(chlorophenyl), ethoxy(fluorophenyl), ethoxy(bromophenyl), ethoxy(iodophenyl), nitrophenyl, aminophenyl, methylaminophenyl, dimethylaminophenyl, ethylaminophenyl, diethylaminophenyl, trimethylammoniumphenyl, triethylammoniumphenyl, trimethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl, triethylammoniumethylcarbonylaminophenyl, trimethylammoniumpropylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl, trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl,

chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, ethylcarbonylaminophenyl, chloroethylcarbonylaminophenyl, fluoroethylcarbonylaminophenyl, bromoethylcarbonylaminophenyl, iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl, chloropropylcarbonylaminophenyl, fluoropropylcarbonylaminophenyl, bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, butylcarbonylaminophenyl, chlorobutylcarbonylaminophenyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl, iodobutylcarbonylaminophenyl, 3,4-dioxymethylenephenyl, pyridinyl, methylpyridinyl, pyridinium, methylpyridinium, thienyl, chlorothienyl, fluorothienyl, bromothienyl, iodothienyl; methoxycarbonylphenyl, ethoxycarbonylphenyl, trimethylammoniumethoxyethoxyethoxyphenyl, triethylammoniumethoxyethoxyethoxyphenyl, chloroethoxyethoxyethoxyphenyl, fluoroethoxyethoxyethoxyphenyl, bromoethoxyethoxyethoxyphenyl, iodoethoxyethoxyethoxyphenyl, pyridiniumethoxyethoxyethoxyphenyl, piperazinyloxymethoxyethoxyethoxyphenyl, methylpiperazinyloxymethoxyethoxyethoxyphenyl, dimethylpiperazinyloxymethoxyethoxyethoxyphenyl, piperidinyloxymethoxyethoxyethoxyphenyl, methylpiperidinyloxymethoxyethoxyethoxyphenyl, and dimethylpiperidinyloxymethoxyethoxyethoxyphenyl; and

R^N is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl and benzyl; and

one or more R^X radicals are independently selected from the group consisting of hydroxy, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, sec-butyl, methoxy, ethoxy, n-propoxy, isopropoxy, methylthio, methylsulfinyl, methylsulfonyl, ethylthio, ethylsulfinyl, ethylsulfonyl,

amino, hydroxyamino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, N-methyl-N-carboxymethyl-amino, N,N-dimethyl-N-carboxymethyl-ammonium, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino, n-propylcarbonylamino, n-butylcarbonylamino, n-pentylcarbonylamino, n-hexylcarbonylamino, benzyloxycarbonylamino, aminoimidocarbonylamino, morpholinyl, N-methyl-morpholinium, azetidinyl, N-methyl-azetidinium, pyrrolidine, N-methyl-pyrrolidinium, piperazinyl, N-methylpiperazinyl, N,N'-dimethyl-piperazinium, piperidinyl, methylpiperidinyl, N-methyl-piperidinium, and thienyl; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

A class of compounds of specific interest comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen and (C_1-C_{10})alkyl; or

R^1 and R^2 taken together with the carbon to which they are attached form (C_3-C_{10})cycloalkyl; and

R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy; and

R^5 is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from the group consisting of halogen; hydroxy; $-NO_2$; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; and $-CONR^9R^{10}$; and

wherein R^9 and R^{10} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; or

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^w and R^{16} are as previously set forth above for the compounds of Formula I; and

R^6 is hydrogen; and

R^N is selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; and aryl(C_1-C_{10})alkyl; and

one or more R^X radicals are independently selected from the group consisting of hydrogen; $-NO_2$; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; $-OR^{13}$; $-NR^{13}R^{14}$;

wherein R^{13} and R^{14} are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

provided that aryl is selected from the group consisting of optionally substituted phenyl, biphenyl and naphthyl; and

provided that heterocyclyl is selected from the group consisting of optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.

A class of compounds of high interest comprises those compounds of Formula I wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of ethyl and n-butyl; or

R^1 and R^2 taken together with the carbon to which they are attached form cyclopentyl; and

one of R^3 and R^4 is hydrogen and the other of R^3 and R^4 is hydroxy; and

R^5 is selected from the group consisting of phenyl, hydroxyphenyl, methoxyphenyl, ethoxyphenyl, nitrophenyl, aminophenyl, methylaminophenyl, dimethylaminophenyl, ethylaminophenyl, diethylaminophenyl, trimethylammoniumphenyl, triethylammoniumphenyl, trimethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl, triethylammoniumethylcarbonylaminophenyl,

trimethylammoniumpropylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl, trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl, chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, ethylcarbonylaminophenyl, chloroethylcarbonylaminophenyl, fluoroethylcarbonylaminophenyl, bromoethylcarbonylaminophenyl, iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl, chloropropylcarbonylaminophenyl, fluoropropylcarbonylaminophenyl, bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, butylcarbonylaminophenyl, chlorobutylcarbonylaminophenyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl, iodobutylcarbonylaminophenyl, trimethylammoniumethoxyethoxyethoxyphenyl, triethylammoniumethoxyethoxyethoxyphenyl, chloroethoxyethoxyethoxyphenyl, fluoroethoxyethoxyethoxyphenyl, bromoethoxyethoxyethoxyphenyl, iodoethoxyethoxyethoxyphenyl, and pyridiniumethoxyethoxyethoxyphenyl; and

R^6 is hydrogen;

R^N is selected from the group consisting of hydrogen, methyl, ethyl, and benzyl; and

one or more R^X radicals are independently selected from the group consisting of hydroxy, methyl, ethyl, methoxy, ethoxy, amino, hydroxyamino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, N-methyl-N-carboxymethyl-amino, N,N-dimethyl-N-carboxymethyl-ammonium, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino,

ethylcarbonylamino, benzyloxycarbonylamino, and aminoimidocarbonylamino; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

A subclass of compounds of high interest comprises those compounds of Formula I wherein:

wherein:

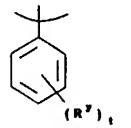
q is 1 or 2;

R^1 and R^2 are each independently alkyl;

R^3 is hydroxy;

R^4 and R^6 are hydrogen;

R^5 has the formula (II):



wherein t is an integer from 0 to 5;

one or more R^y are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y radicals optionally may have one or more carbons replaced by -O-; $-NR^7-$; $-N^+R^7R^8A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^7A^-$; $-PR^7-$; $-P(O)R^7-$; $-P^+R^7R^8A^-$; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$; $-PR^9-$; $-P^+R^9R^{10}A^-$; $-P(O)R^9-$; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as previously set forth above for the compounds of Formula I; and

R^N is selected from the group consisting of hydrogen; alkyl; and aralkyl; and

one or more R^x radicals are independently selected from the group

consisting of alkoxy, alkylamino and dialkylamino; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

A family of specific compounds of particular interest within Formula I consists of the following compounds:

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

5-chloro-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]pentanamide;

5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N*,*N*,*N*-triethyl-5-oxo-pentanaminium trifluoroacetate;

2-chloro-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]acetamide;

2-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N*,*N*,*N*-triethyl-2-oxoethanaminium chloride;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

1-[2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]ethyl]pyridinium;

2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-*N,N,N*-triethylethanaminium iodide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide and (4*S*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin-4-ol 1,1-dioxide;

5-bromo-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl)phenyl]pentanamide;

5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-5-oxo-1-pentanaminium trifluoroacetate;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-*N,N,N*-triethylethanaminium iodide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

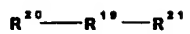
(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5-tetrahydro-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

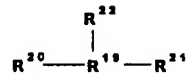
(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide; and

(4*R*,5*R*)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-spiro[1,2-benzothiazepine-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide; and

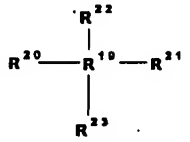
the pharmaceutically-acceptably salts thereof.

The invention further comprises a compound selected from among:


(Formula DI)


(Formula DII),

and


(Formula DIII)

wherein R^{19} is selected from the group consisting of alkane diyl, alkene diyl, alkyne diyl, polyalkane diyl, alkoxy diyl, polyether diyl, polyalkoxy diyl, carbohydrate residue, amino acid residue, peptide residue, and polypeptide residue; and

wherein alkane diyl, alkene diyl, alkyne diyl, polyalkane diyl, alkoxy diyl, polyether diyl, polyalkoxy diyl, carbohydrate residue, amino acid residue, peptide residue, and polypeptide residue optionally may have one or more carbon atoms replaced by -O-, $-NR^7-$, $-N^+R^7R^8A^-$-, -S-, -SO-, $-SO_2-$, $-S^+R^7A^-$-, $-PR^7-$, $-PR^7R^8A^-$-, phenylene, heterocyclyl, quaternary heterocyclyl, or aryl;

wherein alkane diyl, alkene diyl, alkyne diyl, polyalkane diyl, alkoxy diyl, polyether diyl, polyalkoxy diyl, carbohydrate residue, amino acid residue, peptide residue, and polypeptide residue optimally can be substituted with one

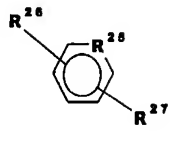
or more radicals independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocyclyl, arylalkyl, halogen, oxo, $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-NO_2$; $-CO_2R^{13}$; -CN; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$;

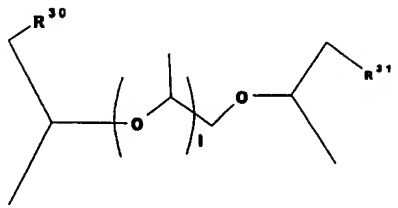
wherein R^{13}, R^{14}, R^{15}, M and A^- are as previously set forth above for the compounds of Formula I; and

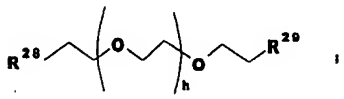
wherein R^{19} can further comprise functional linkages by which R^{19} is bonded to R^{20} and/or R^{21} in the compounds of Formula DI; to R^{20}, R^{21} and/or R^{22} in the compounds of Formula DII; and to R^{20}, R^{21}, R^{22} and/or R^{23} in the compounds of Formula DIII; and

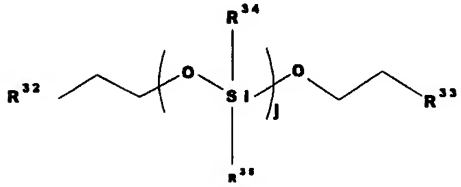
wherein each of R^{20}, R^{21}, or R^{22} and R^{23} comprises a benzothiazepine moiety as described above that is therapeutically effective in inhibiting ileal bile acid transport.

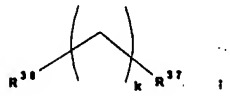
Exemplary R^{19} substituents include, but are not limited to, the following:


;


,



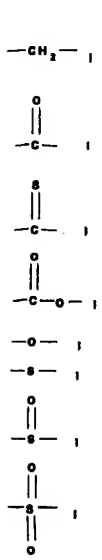


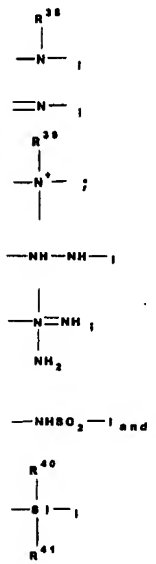


wherein:

R^{25} is selected from the group consisting of carbon and nitrogen; and

R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34}, R^{35}, R^{36}, and R^{37} are independently selected from the group consisting of:



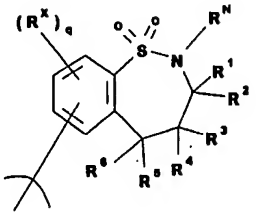


wherein R^{38}, R^{39}, R^{40} and R^{41} are independently selected from the group consisting of alkyl, alkenyl, alkylaryl, aryl, arylalkyl, cycloalkyl, heterocyclyl, and heterocyclylalkyl;

A^- is a pharmaceutically acceptable anion; and

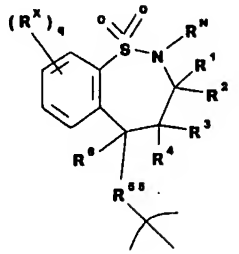
h, i, j and k are independently selected from the group consisting of integers from 1 to 10 inclusive.

The invention is also directed to a compound selected from among Formula DI, Formula DII and Formula DIII in which each of R^{20}, R^{21}, R^{22} and R^{23} comprises a benzothiazepine moiety corresponding to the Formula DIV or Formula DIVA:



(Formula DIV)

or:

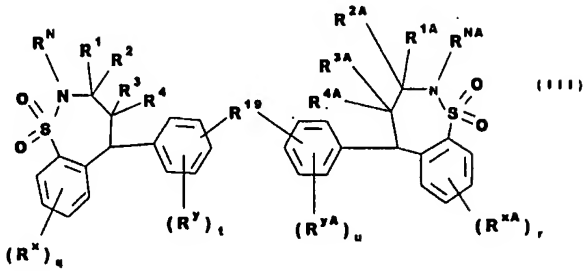


(Formula DIVA)

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^N, R^x, q, and n are as previously defined above for the compounds of Formula I, and R^{55} is either a covalent bond or arylene.

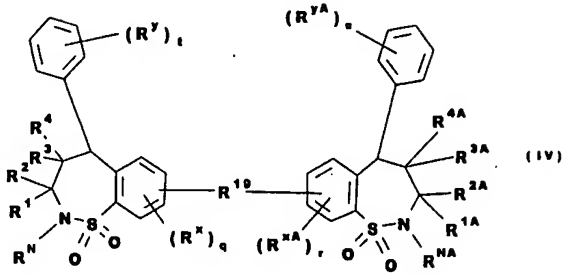
In compounds of Formula DIV, it is particularly preferred that each of R^{20}, R^{21}, R^{22}, and R^{23} in Formulae DI, DII and DIII be bonded at its 7- or 8-position to R^{19}. In compounds of Formula DIVA, it is particularly preferred that R^{55} comprise a phenylene moiety bonded at a *m*- or *p*-carbon thereof to R^{19}.

Examples of Formula DI include:



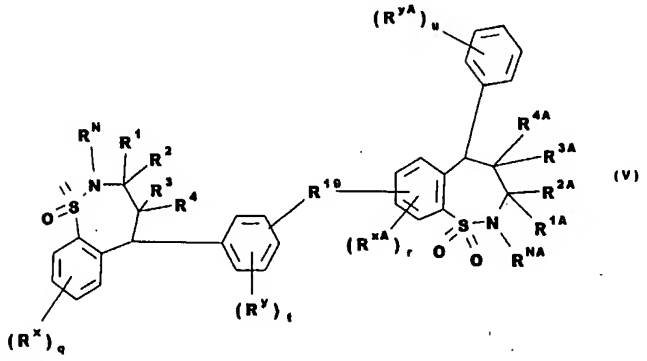
(III)

and



(IV)

and

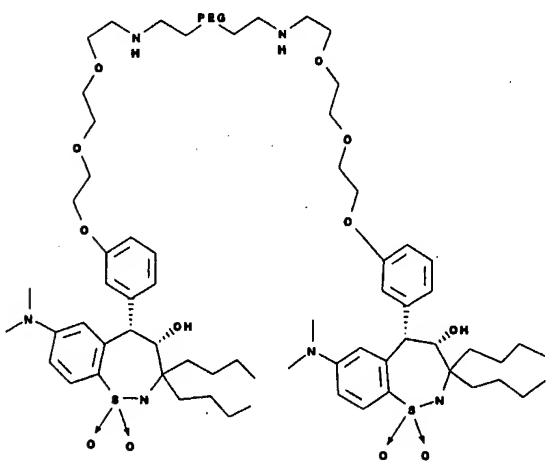


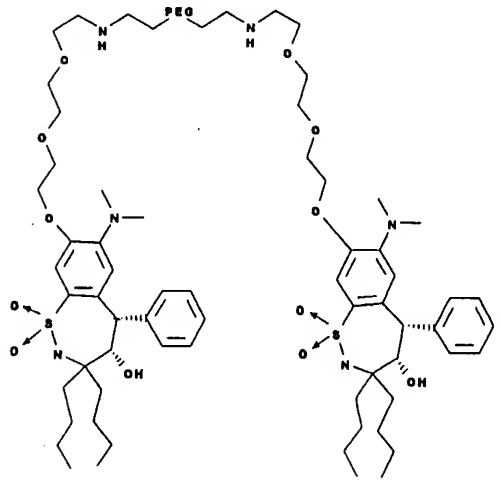
(V)

wherein R^{1A}, R^{2A}, R^{3A}, R^{4A}, R^{NA}, R^{yA}, R^{xA}, r and u have the same definitions as stated above for R^1, R^2, R^3, R^4, R^{NA}, R^y, R^x, q and t, respectively.

In any of the compounds of the present invention, R^1 and R^2 can be, among other combinations, ethyl/butyl or butyl/butyl.

Illustrative dimeric compounds include the following:





In another embodiment, a core moiety backbone, R^{19}, as discussed herein in Formulae DI, DII and DIII can be multiply substituted with more than four pendant active benzothiazepine units, i.e., R^{20}, R^{21}, R^{22}, and R^{23} as discussed above, through multiple functional groups within the core moiety backbone. The core moiety backbone unit, R^{19}, can comprise a single core moiety unit, multimers thereof, and multimeric mixtures of the different core moiety units discussed herein, i.e., alone or in combination. The number of individual core moiety backbone units can range from about one to about 100, preferably about one to about 80, more preferably about one to about 50, and even more preferably about one to about 25. The number of points of attachment of similar or different pendant active benzothiazepine units within a single core moiety backbone unit can be in the range from about one to about 100, preferably about one to about 80, more preferably about one to about 50, and even more preferably about one to about 25. Such points of attachment can include bonds to C, S, O, N, or P within any of the groups encompassed by the definition of R^{19}.

The more preferred benzothiazepine moieties comprising R^{20}, R^{21}, R^{22} and/or R^{23} conform to the preferred structures as outlined above for Formula I. The 3-position carbon on each benzothiazepine moiety can be achiral, and the substituents R^1, R^2, R^3, R^4, R^5 and R^6 can be selected from the preferred groups and combinations of substituents as discussed above. The core structures can comprise, for example, poly(oxyalkylene) or oligo(oxyalkylene), especially poly- or oligo(oxyethylene) or poly- or oligo(oxypropylene).

Methods of Treatment

In another aspect, the present invention provides a pharmaceutical composition for the prophylaxis and/or treatment of a disease, condition and/or disorder for which a bile acid transport inhibitor is indicated, such as a hyperlipidemic condition, for example, atherosclerosis. Such compositions

comprise any of the compounds disclosed above, alone or in combination, in an amount effective to reduce bile acid levels in the blood, or to reduce transport thereof across digestive system membranes, alone or in a composition comprising, for example, one or more pharmaceutically acceptable carriers, excipients, and/or diluents. In any of the dimeric or multimeric structures discussed immediately above, for example, the benzothiazepine compounds of the present invention can be used alone or in various combinations.

In a further aspect, the present invention also provides a method of treating a disease, condition and/or disorder in mammals, including humans, for which a bile acid transport inhibitor is indicated, comprising administering to a patient in need thereof a compound of the present invention in an effective amount in unit dosage form or in divided doses.

In yet a further aspect, the present invention comprises the use of the compounds of Formula I and/or the dimeric or multimeric compounds of Formulae DI, DII and/or DIII in the preparation of a medicament useful for the prophylaxis and/or treatment of a disease, condition and/or disorder for which a bile acid transport inhibitor is indicated.

The compounds of Formula I are also useful for the prophylaxis and/or treatment of gallstones.

In yet a further aspect, the present invention also provides processes for the preparation of compounds of the present invention.

Further scope of the applicability of the present invention will become apparent from the detailed description provided below. However, it should be understood that the following detailed description and examples, while indicating preferred embodiments of the invention, are given by way of illustration only since various changes and modifications within the spirit and scope of the invention will beomce apparent to those skilled in the art from this detailed description.

Definitions and Abbreviations

In order to aid the reader in understanding the following detailed description, the following definitions are provided:

The term "hydrocarbyl" refers to radicals consisting exclusively of the elements carbon and hydrogen. These radicals include, for example, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, and aryl moieties. These radicals also include alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, and aryl moieties substituted with other aliphatic or cyclic hydrocarbon groups, such as alkaryl, alkenaryl and alkynaryl. Preferably, these moieties comprise 1 to 20 carbon atoms.

The term "substituted hydrocarbyl" refers to a hydrocarbyl radical that is substituted with a group comprising at least one atom other than carbon, such as but not limited to, halogen, oxygen, nitrogen, sulfur and phosphorus. Examples of such substituted hydrocarbyl include hydrocarbyl radicals substituted with groups such as, but not limited to, lower alkoxy such as methoxy, ethoxy, and butoxy; halogen such as chloro and fluoro; ethers; acetals; ketals; esters; heterocyclyl such as furyl and thienyl; alkanoxy; hydroxy; protected hydroxy; acyl; acyloxy; nitro; cyano; amino; and amido. Substituted hydrocarbyl also includes hydrocarbyl radicals in which a carbon chain atom is replaced with a heteroatom such as nitrogen, oxygen, sulfur, or a halogen.

Where the term "alkyl" is used, either alone or within other terms such as "haloalkyl", and "hydroxyalkyl", it embraces linear or branched radicals having one to about twenty carbon atoms or, preferably, one to about twelve carbon atoms. More preferred alkyl radicals are "lower alkyl" radicals having one to about six carbon atoms. Examples of such radicals include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, iso-amyl, hexyl and the like. Even more preferred are lower alkyl radicals having one to three carbon atoms.

Where the term "alkenyl" is used, either alone or within other terms such as "arylalkenyl", it embraces linear or branched radicals having at least

one carbon-carbon double bond of two to about twenty carbon atoms or, preferably, two to about twelve carbon atoms. More preferred alkenyl radicals are "lower alkenyl" radicals having two to about six carbon atoms. Examples of alkenyl radicals include ethenyl, propenyl, allyl, propenyl, butenyl and 4-methylbutenyl.

The terms "alkenyl" and "lower alkenyl", embrace radicals having "cis" and "trans" orientations, or alternatively, "E" and "Z" orientations.

The term "alkynyl" denotes linear or branched radicals having two to about twenty carbon atoms or, preferably, two to about twelve carbon atoms. More preferred alkynyl radicals are "lower alkynyl" radicals having two to about ten carbon atoms. Most preferred are lower alkynyl radicals having two to about six carbon atoms. Examples of such radicals include propargyl, butynyl, and the like.

The term "cycloalkyl" embraces saturated carbocyclic radicals having three to about twelve carbon atoms. More preferred cycloalkyl radicals are "lower cycloalkyl" radicals having three to about ten carbon atoms. Examples of such radicals include cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. The term "cycloalkyl" additionally encompasses spiro systems wherein the cycloalkyl ring has a carbon ring atom in common with the seven-membered heterocyclic ring of the benzothiazepine.

The term "cycloalkenyl" embraces partially unsaturated carbocyclic radicals having three to twelve carbon atoms. Cycloalkenyl radicals that are partially unsaturated carbocyclic radicals that contain two double bonds (that may or may not be conjugated) can be called "cycloalkyldienyl". More preferred cycloalkenyl radicals are "lower cycloalkenyl" radicals having four to about ten carbon atoms. Examples of such radicals include cyclobutenyl, cyclopentenyl and cyclohexenyl.

The term "halo" and "halogen" means halogens such as fluorine, chlorine, bromine or iodine atoms. The term "haloalkyl" embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with halo as

defined above. Specifically embraced are monohaloalkyl, dihaloalkyl and polyhaloalkyl radicals. A monohaloalkyl radical, for one example, may have either an iodo, bromo, chloro or fluoro atom within the radical. Dihalo and polyhaloalkyl radicals may have two or more of the same halo atoms or a combination of different halo radicals. "Lower haloalkyl" embraces radicals having one to six carbon atoms. Examples of haloalkyl radicals include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl. "Perfluoroalkyl" means alkyl radicals having all hydrogen atoms replaced with fluoro atoms. Examples include trifluoromethyl and pentafluoroethyl.

The term "hydroxyalkyl" embraces linear or branched alkyl radicals having one to about ten carbon atoms any one of which may be substituted with one or more hydroxyl radicals. More preferred hydroxyalkyl radicals are "lower hydroxyalkyl" radicals having one to six carbon atoms and one or more hydroxyl radicals. Examples of such radicals include hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl and hydroxyhexyl. Even more preferred are lower hydroxyalkyl radicals having one to three carbon atoms.

The term "aryl", alone or in combination, means a carbocyclic aromatic system containing one or more rings wherein such rings may be attached together in a pendent manner or may be fused. The term "aryl" embraces aromatic radicals such as phenyl, naphthyl, tetrahydronaphthyl, indane, biphenyl, and anthracenyl. More preferred aryl is phenyl. Said "aryl" group may have one to three substituents such as lower alkyl, hydroxy, halo, haloalkyl, nitro, cyano, alkoxy and lower alkylamino.

The term "heterocyclyl" embraces saturated, partially saturated and unsaturated heteroatom-containing ring-shaped radicals, where the heteroatoms may be selected from nitrogen, sulfur and oxygen. Preferred heterocyclyl are 3-10 membered ring heterocyclyl, particularly 5-8 membered ring heterocyclyl.

Examples of saturated heterocyclic radicals include saturated 3 to 6-membered heteromonocyclic groups containing 1 to 4 nitrogen atoms [e.g. pyrrolidinyl, imidazolidinyl, piperidino, piperazinyl]; saturated 3 to 6-membered heteromonocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. morpholinyl]; saturated 3 to 6-membered heteromonocyclic groups containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiazolidinyl]. Examples of partially saturated heterocyclyl radicals include dihydrothiophene, dihydropyran, dihydrofuran and dihydrothiazole. Examples of unsaturated heterocyclic radicals, also termed "heteroaryl" radicals, include unsaturated 5 to 6 membered heteromonocyclyl groups containing 1 to 4 nitrogen atoms, for example, pyrrolinyl, imidazolyl, pyrazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl [e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl]; unsaturated condensed heterocyclic groups containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g., tetrazolo [1,5-b]pyridazinyl]; unsaturated 3 to 6-membered heteromonocyclic groups containing an oxygen atom, for example, pyranyl, 2-furyl, 3-furyl, etc.; unsaturated 5 to 6-membered heteromonocyclic groups containing a sulfur atom, for example, 2-thienyl, 3-thienyl, etc.; unsaturated 5- to 6-membered heteromonocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, isoxazolyl, oxadiazolyl [e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl]; unsaturated condensed heterocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzoxazolyl, benzoxadiazolyl]; unsaturated 5 to 6-membered heteromonocyclic groups containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, thiadiazolyl [e.g., 1,2,4- thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl]; unsaturated condensed heterocyclic groups containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl] and the like. The term also embraces radicals where heterocyclic radicals are fused with aryl radicals. Examples of

such fused bicyclic radicals include benzofuran, benzothiophene, and the like. Said "heterocyclyl" group may have 1 to 3 substituents such as lower alkyl, hydroxy, oxo, amino and lower alkylamino.

Heterocyclic radicals can include fused or unfused radicals, particularly 3-10 membered fused or unfused radicals. Preferred examples of heteroaryl radicals include benzofuryl, 2,3-dihydrobenzofuryl, benzothienyl, indolyl, dihydroindolyl, chromanyl, benzopyran, thiochromanyl, benzothiopyran, benzodioxolyl, benzodioxanyl, pyridyl, thienyl, thiazolyl, furyl, and pyrazinyl. More preferred heteroaryl radicals are 5- or 6-membered heteroaryl, containing one or two heteroatoms selected from sulfur nitrogen and oxygen, selected from thienyl, furanyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, pyridyl, piperidinyl and pyrazinyl.

The term "heteroaryl" means a fully unsaturated heterocyclyl.

In either "heterocyclyl" or "heteroaryl," the point of attachment to the molecule of interest can be at the heteroatom or elsewhere within the ring.

The term "triazolyl" includes all positional isomers. In all other heterocyclyl and heteroaryl which contain more than one ring heteroatom and for which isomers are possible, such isomers are included in the definition of said heterocyclyl and heteroaryl.

The term "quaternary heterocyclyl" means a heterocyclyl in which one or more of the heteroatoms, for example, nitrogen, sulfur, phosphorus or oxygen, has such a number of bonds that it is positively charged (and therefore the term is intended to encompass both ternary and quaternary positively charged structures). The point of attachment of the quaternary heterocyclyl to the molecule of interest can be at a heteroatom or elsewhere.

The term "quaternary heteroaryl" means a heteroaryl in which one or more of the heteroatoms, for example, nitrogen, sulfur, phosphorus or oxygen, has such a number of bonds that it is positively charged (and therefore the term is intended to encompass both ternary and quaternary positively charged structures). The point of attachment of the quaternary heteroaryl to the

molecule of interest can be at a heteroatom or elsewhere.

The term "diyl" means a diradical moiety wherein said moiety has two points of attachment to molecules of interest.

The term "oxo" means a doubly bonded oxygen.

The term "polyalkyl" means a branched or straight hydrocarbon chain having a molecular weight up to about 20,000, more preferably up to about 10,000, and most preferably up to about 5,000.

The term "polyether" means a polyalkyl wherein one or more carbons are replaced by oxygen, wherein the polyether has a molecular weight up to about 20,000, more preferably up to about 10,000, and most preferably up to about 5,000.

The term "polyalkoxy" means a polymer of alkylene oxides, wherein the polyalkoxy has a molecular weight up to about 20,000, more preferably up to about 10,000, and most preferably up to about 5,000.

The term "carbohydrate residue" encompasses residues derived from carbohydrates such as, but is not limited to, mono-, di-, tri-, tetra- and polysaccharides wherein the polysaccharides can have a molecular weight of up to about 20,000, for example, hydroxypropyl-methylcellulose or chitosan residue; compounds derived from aldoses and ketoses with 3 to 7 carbon atoms and which belong to the D- or L-series; aminosugars; sugar alcohols; and saccharic acids. Nonlimiting specific examples of such carbohydrates include glucose, mannose, fructose, galactose, ribose, erythrose, glycerinaldehyde, sedoheptulose, glucosamine, galactosamine, glucoronic acid, galacturonic acid, gluconic acid, galactonic acid, mannoic acid, glucamine, 3-amino-1,2-propanediol, glucaric acid and galactaric acid.

The term "peptide residue" means polyamino acid residue containing up to about 100 amino acid units.

The term "polypeptide residue" means a polyamino acid residue containing from about 100 amino acid units to about 1000 amino acid units, more preferably from about 100 amino acid units to about 750 amino acid

untis, and most preferably from about 100 amino acid units to about 500 amino acid units.

The term "alkylammoniumalkyl" means an an -NH_2 group or a mono-, di- or tri-substituted amino group, any of which is bonded to an alkyl wherein said alkyl is bonded to the molecule of interest.

The term "sulfo" means a sulfo group, -SO_3H, and its salts.

The term "sulfoalkyl" means an alkyl group to which a sulfonate group is bonded, wherein said alkyl is bonded to the molecule of interest.

The term "aralkyl" embraces aryl-substituted alkyl radicals. Preferable aralkyl radicals are "lower aralkyl" radicals having aryl radicals attached to alkyl radicals having one to six carbon atoms. Even more preferred are lower aralkyl radicals having phenyl attached to alkyl portions having one to three carbon atoms. Examples of such radicals include benzyl, diphenylmethyl and phenylethyl. The aryl in said aralkyl may be additionally substituted with halo, alkyl, alkoxy, halkoalkyl and haloalkoxy. The term "arylalkenyl" embraces aryl-substituted alkenyl radicals. Preferable arylalkenyl radicals are "lower arylalkenyl" radicals having aryl radicals attached to alkenyl radicals having

The term "heterocyclylalkyl" means an alkyl radical that is substituted with one or more heterocyclyl groups. Preferable heterocyclylalkyl radicals are "lower heterocyclylalkyl" radicals having one or more heterocyclyl groups attached to an alkyl radical having one to ten carbon atoms.

The term "heteroarylalkyl" means an alkyl radical that is substituted with one or more heteroaryl groups. Preferable heteroarylalkyl radicals are "lower heteroarylalkyl" radicals having one or more heteroaryl groups attached to an alkyl radical having one to ten carbon atoms.

The term "quaternary heterocyclylalkyl" means an alkyl radical that is substituted with one or more quaternary heterocyclyl groups. Preferable quaternary heterocyclylalkyl radicals are "lower quaternary heterocyclylalkyl" radicals having one or more quaternary heterocyclyl groups attached to an alkyl radical having one to ten carbon atoms.

The term "quaternary heteroarylalkyl" means an alkyl radical that is substituted with one or more quaternary heteroaryl groups. Preferable quaternary heteroarylalkyl radicals are "lower quaternary heteroarylalkyl" radicals having one or more quaternary heteroaryl groups attached to an alkyl radical having one to ten carbon atoms.

The term "alkylheteroarylalkyl" means a heteroarylalkyl radical that is substituted with one or more alkyl groups. Preferable alkylheteroarylalkyl radicals are "lower alkylheteroarylalkyl" radicals with alkyl portions having one to ten carbon atoms.

The term "alkoxy" means an alkyl radical which is attached to the molecule of interest by oxygen, such as a methoxy radical. More preferred alkoxy radicals are "lower alkoxy" radicals having one to six carbon atoms. Examples of such radicals include methoxy, ethoxy, propoxy, iso-propoxy, butoxy and *tert*-butoxy.

The term "carboxy" means the carboxy group, -CO_2H, or its salts.

The term "carboxyalkyl" means an alkyl radical that is substituted with one or more carboxy groups. Preferable carboxyalkyl radicals are "lower carboxyalkyl" radicals having one or more carboxy groups attached to an alkyl radical having one to six carbon atoms.

The term "carboxyheterocyclyl" means a heterocyclyl radical that is substituted with one or more carboxy groups.

The term "carboxyheteroaryl" means a heteroaryl radical that is substituted with one or more carboxy groups.

The term "carboalkoxyalkyl" means an alkyl radical that is substituted with one or more alkoxycarbonyl groups. Preferable carboalkoxyalkyl radicals are "lower carboalkoxyalkyl" radicals having one or more alkoxycarbonyl groups attached to an alkyl radical having one to six carbon atoms.

The term "carboxyalkylamino" means an amino radical that is mono- or di-substituted When used in combination, for example "alkylaryl" or "arylalkyl," the individual terms listed above have the meaning indicated

above.

The term "acyl" means an organic acid group in which the hydroxy of the carboxy group has been removed. Examples of acyl groups include, but are not limited to, acetyl and benzoyl.

The term "active compound" means a compound of the present invention that inhibits transport of bile acids.

The term "a bile acid transport inhibitor" means a compound capable of inhibiting absorption of bile acids from the intestine into the circulatory system of a mammal, such as a human. This includes increasing the fecal excretion of bile acids, as well as reducing the blood plasma or serum concentrations of cholesterol and cholesterol ester, and more specifically, reducing LDL and VLDL cholesterol. Conditions and/or diseases that benefit from the prophylaxis and/or treatment by bile acid transport inhibition include, for example, a hyperlipidemic condition such as atherosclerosis.

The abbreviations used in this application have the following meanings:

The term "THF" means tetrahydrofuran;

The term "PTC" means phase transfer catalyst;

The term "Aliquart 336" means methyltricaprylylammonium chloride;

The term "MCPBA" means m-chloroperbenzoic acid;

The term "Celite" refers to a brand of diatomaceous earth filtering aid;

The term "DMF" means dimethylformamide;

The term "DME" means ethylene glycol dimethyl ether;

The term "BOC" means t-butoxycarbonyl;

The term "Me" means methyl;

The term "Et" means ethyl;

The term "Bu" means butyl;

The term "EtOAc" means ethyl acetate;

The term "Et_2O" means diethyl ether;

The term "LAH" means lithium aluminum hydride;

The term "DMSO" means dimethylsulfoxide;

The term "$KOSiMe_3$" means potassium trimethylsilanolate;

The term "PEG" means polyethylene glycol;

The term "MS" means mass spectrometry;

The term "HRMS" means high resolution mass spectrometry;

The term "ES" means electrospray;

The term "NMR" means nuclear magnetic resonance spectroscopy;

The term "GC" means gas chromatography;

The term "MPLC" means medium pressure liquid chromatography;

The term "HPLC" means high pressure liquid chromatography;

The term "RPHPLC" means reverse phase high pressure liquid chromatography

The term "RT" means room temperature;

The terms "h" or "hr" means hour(s); and

The term "min" means minute(s);

Alternate Forms of Compounds

The compounds of the present invention can have at least two asymmetrical carbon atoms, and therefore include racemates and stereoisomers, such as diastereomers and enantiomers, in both pure form and in admixture. Such stereoisomers can be prepared and separated using conventional techniques, either by reacting enantiomeric starting materials, or by separating isomers of compounds of the present invention. Isomers may include geometric isomers, for example cis isomers or trans isomers across a double bond. All such isomers are contemplated among the compounds of the present invention.

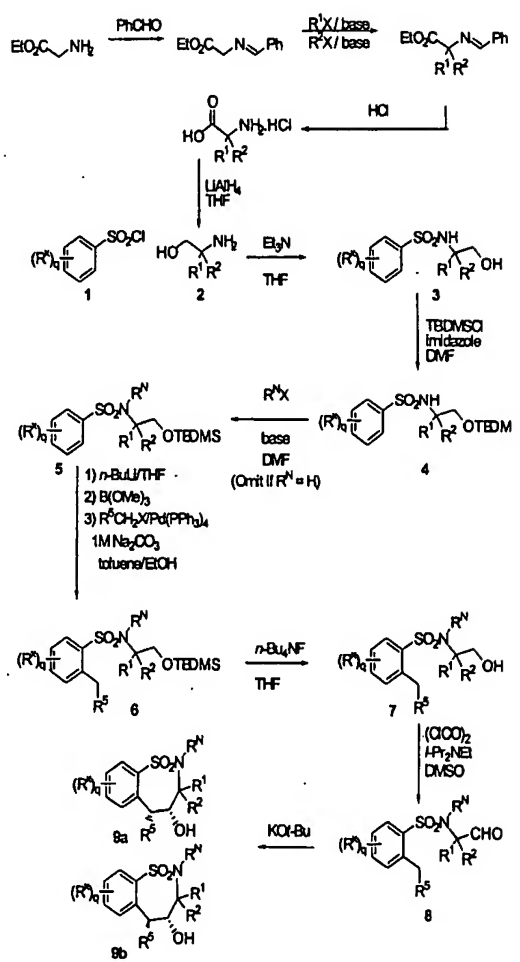
The compounds of the present invention also include tautomers, salts, solvates and prodrugs of such compounds.

Compound Syntheses

The starting materials for use in the preparation of the compounds of the invention are commercially available or can be prepared by conventional methods known to a skilled person or in an analogous manner to processes described in the art.

Generally, the compounds of the present invention can be prepared by the procedures described below.

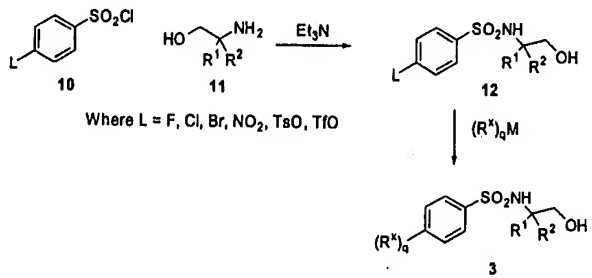
Scheme 1



Scheme 1 illustrates the preparation of racemic benzothiazepines 9a and 9b. Reaction of benzenesulfonyl chloride 1 with aminoalcohol 2 in the presence of a base, such as triethylamine, in a solvent, such as tetrahydrofuran, yields benzenesulfonamide 3 which can be converted to protected benzenesulfonamide 4. Protected benzenesulfonamide 4 optionally can be treated with an alkyl halide, such as methyl iodide, in the presence of a base such as sodium hydride, in a solvent, such as dimethylformamide, to yield N-substituted benzenesulfonamide 5. Protected benzenesulfonamide 4 or N-substituted benzenesulfonamide 5 is then successively reacted with (i) a strong base (such as n-butyllithium in hexanes) in a solvent (such as tetrahydrofuran), (ii) an electrophile (such as trimethyl borate), and (iii) a base (such as sodium carbonate), a benzyl halide (such as p-methoxybenzyl chloride), and a catalyst (such as tetrakis(triphenylphosphine)palladium(0)) to yield sulfonamide 6. Treatment of sulfonamide 6 with a fluoride source, such as tetrabutylammonium fluoride, in a solvent, such as tetrahydrofuran, provides the deprotected sulfonamide alcohol 7. Sulfonamide alcohol 7 is successively oxidized using a method such as Swern Oxidation to yield sulfonamide aldehyde 8. Upon treatment with a base such as potassium tert-butoxide, aldehyde 8 is converted to racemic benzothiazepines 9a and 9b. R^1, R^2, R^5, R^N, R^x and q are as previously defined above for compounds of Formula I.

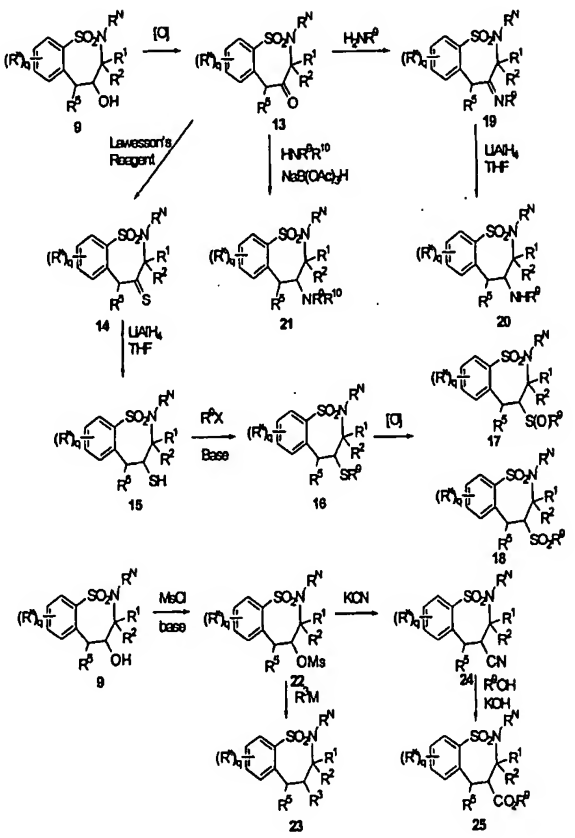
SCHEME 2

Alternative Synthesis of sulfonamide alcohol



Scheme 2 illustrates an alternative synthetic scheme for the preparation of sulfonamide alcohol 3 used in Scheme 1. Reaction of benzenesulfonyl chloride 10 with aminoalcohol 11 in the presence of a base, such as triethylamine, in a solvent, such as tetrahydrofuran, yields sulfonamide 12. Substituent L of benzenesulfonyl chloride 10 is a suitable leaving group such as fluoro, chloro, bromo, nitro, tosyloxy or trifluoromethylsulfonyloxy. Reaction of sulfonamide 12 with a suitable nucleophile in the presence of a base, such as triethylamine, in a solvent, such as tetrahydrofuran, yields benzenesulfonamide 3 which can be further reacted in accordance with Scheme 1. R^1, R^2, R^x and q are as previously defined above for compounds of Formula I. Substituent M is a metal, preferably an alkali metal, or a hydrogen.

SCHEME 3



Scheme 3 illustrates the preparation of benzothiazepines having 4-position substituents other than hydroxy.

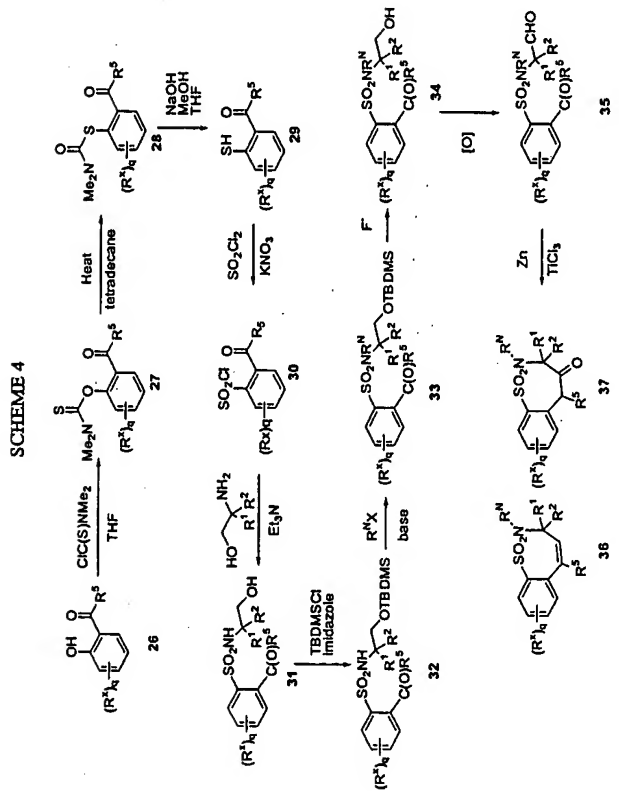
In the preparation of 4-thioxo-, thio-, sulfinyl- or sulfonyl-benzothiazepines, benzothiazepine **9a** or **9b** is first oxidized to benzothiazepine-4-one **13**. Conventional oxidizing agents, such as PCC, or Swern conditions can be used. Benzothiazepine-4-one **13** is then reacted with Lawesson's Reagent to produce 4-thioxo-benzothiazepine **14**. 4-Thioxo-benzothiazepine **14** can be reacted with a suitable reducing agent, such as lithium aluminum hydride, in a suitable solvent, such as tetrahydrofuran, to yield 4-mercapto-benzothiazepine **15**. 4-Mercapto-benzothiazepine **15** can be reacted with a suitable alkylating agent, such as an alkyl halide, in the presence of a base, such as sodium hydride, in a suitable solvent, such as dimethylformamide, to yield 4-alkylthio-benzothiazepine **16**. 4-Alkylthio-benzothiazepine **16** can be reacted with a suitable oxidizing agent, such as *t*-butyl hydroperoxide or *m*-chloroperbenzoic acid, to yield, successively, 4-alkylsulfinyl-benzothiepine **17** and 4-alkylsulfonyl-benzothiazepine **18**.

Alternatively, 4-amino- or imino-benzothiazepines can be prepared by reacting benzothiazepine-4-one **13** with ammonia or a primary amine in a suitable solvent, such as tetrahydrofuran, to produce 4-imino-benzothiazepine **19**. 4-Imino-benzothiazepine **19** can be reacted with a suitable reducing agent, such as lithium aluminum hydride, in a suitable solvent, such as tetrahydrofuran, to yield 4-amino-benzothiazepine **20**. Benzothiazepine-4-one **13** also can undergo reductive alkylation by reaction with ammonia, a primary amine or a secondary amine in the presence of an reducing agent, such as sodium triacetoxyborohydride, in a suitable solvent, such as tetrahydrofuran, to produce 4-amino-benzothiazepine **21**.

Scheme 3 also illustrates the preparation of 4-alkyl-benzothiazepine **23** and 4-alkoxycarbonyl-benzothiazepine **25**. The 4-position hydroxy of benzothiazepine **9a** or **9b** is first converted to a suitable leaving group such as mesyloxy to form protected benzothiazepine **22**. Protected benzothiazepine **22**

is then reacted with a suitable nucleophile, such as butyl lithium, in a suitable solvent, such as tetrahydrofuran, to yield 4-alkyl-benzothiazepine **23**. Alternatively, protected benzothiazepine **22** can be reacted with a suitable cyanidating agent, such as an potassium cyanide, in a suitable solvent, such as dimethylformamide, to yield 4-cyano-benzothiazepine **24**. 4-Cyano-benzothiazepine **24** is converted to 4-alkoxycarbonyl-benzothiazepine **25** by reaction with a suitable alcohol in the presence of a base, such as potassium hydroxide.

SCHEME 4



Scheme 4 illustrates the preparation of benzothiazepine-4-ene 36 and benzothiazepine-4-one 33. Reaction of phenol 26 with a thiocarbamyl chloride, such as dimethylthiocarbamyl chloride, in a solvent, such as methanol:tetrahydrofuran yields *O*-thiocarbamate 27. Heating of *O*-thiocarbamate 27 in a solvent, such as tetradecane, yields *S*-thiocarbamate 28. Hydrolysis of *S*-thiocarbamate 28 in the presence of a base, such as sodium hydroxide, in a solvent, such as methanol:tetrahydrofuran, yields thiophenol 29. Thiophenol 29 can be treated with a sulfonylating agent, such as sulfonyl chloride, in the presence of a oxidant such as potassium nitrate, in a solvent, such as tetrahydrofuran, to yield sulfonyl chloride 30. Sulfonyl chloride 30 is then reacted with an aminoalcohol in a solvent, such as tetrahydrofuran, to yield benzenesulfonamide 31. Benzenesulfonamide 31 optionally can be hydroxyl protected with a silylating group agent, such as *tert*-butyldimethylsilyl chloride, in the presence of a base, such as imidazole, in a solvent, such as tetrahydrofuran, to yield protected benzenesulfonamide 32. Protected benzenesulfonamide 32 can be treated with an alkyl halide, such as methyl iodide, in the presence of a base such as sodium hydride, in a solvent, such as dimethylformamide, to yield N-substituted benzenesulfonamide 33. Deprotection of the protected N-substituted benzene sulfonamide 33 with a fluoride source, such as tetrabutylammonium fluoride, in a solvent, such as tetrahydrofuran, yields N-substitued benzenesulfonamide 34. Benzenesulfonamide 31 or N-substituted benzenesulfonamide 34 is then oxidized with a suitable oxidizing agent or under Swern conditions to form aldehyde 35. Upon treatment with zinc and titanium trichloride aldehyde 35 is converted to a mixture of benzothiazepine-4-ene 36 and benzothiazepine-4-one 37.

The recovery, isolation and purification of the intermediates and the reaction products of this invention, and in particular the intermediates and the reaction products illustrated in Schemes 1, 2, 3 and 4, can be accomplished by conventional methods well known to those skilled in the art, such as

precipitation, filtration, extraction, or chromatography. Except where otherwise indicated, conditions, solvents, and reagents are either conventional, not narrowly critical, or both.

Additional Embodiments and Examples

Another class of compounds of specific interest comprises those compounds of Formula I wherein R^1 and R^2 are selected from among substituted and unsubstituted C_{1-10} alkyl wherein substituted C_{1-10} alkyl comprises one or more radicals independently selected from among, for example, alkylcarbonyl, alkoxy, hydroxy, and nitrogen-containing heterocyclyl joined to the C_{1-10} alkyl through an ether linkage. These R^1 and R^2 substituents include ethyl, n-propyl, n-butyl, n-pentyl, isobutyl, isopropyl, $-CH_2C(=O)C_2H_5$, $-CH_2OC_2H_5$, and $-CH_2$ O-(4-picoline). Ethyl, n-propyl, n-butyl, and isobutyl are preferred. In certain particularly preferred compounds of the present invention, substituents R^1 and R^2 are identical, for example n-butyl/n-butyl, so that the compound is achiral at the 3-position carbon. Eliminating optical isomerism at the 3-position carbon simplifies the selection, synthesis, separation, and quality control of the compound used as an ileal bile acid transport inhibitor.

In the compounds of the present invention having a chiral 3-position carbon as well as those having an achiral 3-position carbon, substituents R^5 on the benzo ring can include, for example, hydrogen, aryl, alkyl, hydroxy, halo, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkyl, haloalkoxy, (N)-hydroxy-carbonylalkylamino, haloalkylthio, haloalkylsulfinyl, haloalkylsufonyl, amino, N-alkylamino, N,N-dialkylamino, (N)-alkoxycarbamoyl, (N)-aryloxycarbamoyl, (N)-aralkyloxycarbamoyl, trialkylammonium (especially with a halide counterion), (N)-amido, (N)-alkylamido, N,N-dialkylamido, (N)-haloalkylamido, (N)-sulfonamido, (N)-alkylsulfonamido, (N)-haloalkylsulfonamido, carboxyalkylamino, trialkylammonium salt, (N)-carbamic acid, alkyl or benzyl ester, N-acylamino,

hydroxylamino, haloacylamino, carbohydrate residue, thiophene, a trialkyl ammonium salt having a carboxylic acid or hydroxy substituent on one or more of the alkyl substituents, an alkylene bridge having a quaternary ammonium salt substituted thereon, -[O(CH2)$_d$] $_e$-X where e is 2 to 12, d is 2 or 3 and X is a halo or a quaternary ammonium salt, and (N)-nitrogen containing heterocyclyl wherein the nitrogen of said heterocyclyl is optionally quaternized.

Among the preferred species which may constitute R^5 are methyl, ethyl, isopropyl, t-butyl, hydroxy, methoxy, ethoxy, isopropoxy, methylthio, iodo, bromo, fluoro, methylsulfinyl, methylsulfonyl, ethylthio, amino, hydroxylamino, N-methylamino, N,N-dimethylamino, N,N-diethylamino, (N)-benzyloxycarbamoyl, trimethylammonium A$^-$, -NHC(=O)CH_3, -NHC(=O)C_5H_{11} , -NHC(=O)C_6H_{13}, carboxyethylamino, (N)-morpholinyl, (N)-azetidinyl, (N)-N-methylazetidinium A-, (N)-pyrrolidinyl, pyrrolyl, (N)-N-methylpyridinium A-, (N)-N-methylmorpholinium A-, and N-N'-methylpiperazinyl, (N)-bromomethylamido, (N)-N-hexylamino, thiophene, -N+$(CH_3)_2$ CO_2 H I$^-$, -NCH_3 CH_2 CO_2H, -(N)-N'-dimethylpiperazinium I$^-$, (N)-t-butyloxycarbamoyl, (N)-methylsulfonamido, (N)N'-methylpyrrolidinium, and -$(OCH_2CH_2)_3$I, where A$^-$ is a pharmaceutically acceptable anion.

The benzo ring can be mono-substituted at the 6, 7 or 8 position, or disubstituted at the 7- and -8 positions. Also included are the 6,7,8-trialkoxy compounds, for example the 6,7,8-trimethoxy compounds. A variety of other substituents can be advantageously present on the 6, 7, 8, and/or 9- positions of the benzo ring including, for example, guanidinyl, cycloalkyl, carbohydrate residue (e.g., a 5 or 6 carbon monosaccharide residue), peptide residue, and quaternary ammonium salts linked to the ring via poly(oxyalkylene) linkages, e.g., -(OCH_2 CH_2)$_x$ -N+R ^{13}R^{14}R^{15}A$^-$, where x is 2 to 10.

In further compounds of the present invention, R^5 and R^6 are independently selected from among hydrogen and ring-carbon substituted or unsubstituted aryl, thiopene, pyridine, pyrrole, thiazole, imidazole, pyrazole,

pyrimidine, morpholine, N-alkylpyridinium, N-alkylpiperazinium, N-alkylmorpholinium, or furan in which the substituent(s) are selected from among, for example, halo, hydroxyl, trihaloalkyl, alkoxy, amino, N-alkylamino, N,N-dialkylamino, quaternary ammonium salts, a C_1 to C_4 alkylene bridge having a quaternary ammonium salt substituted thereon, alkoxycarbonyl, aryloxycarbonyl, alkylcarbonyloxy and arylcarbonyloxy, (O,O)-dioxyalkylene, -[O(CH_2)$_d$]$_e$X where e is 2 to 12, d is 2 or 3 and x comprises halo or a quaternary ammonium salt, thiophene, pyridine, pyrrole, thiazole, imidazole, pyrazole, or furan. The aryl group of R^5 or R^6 is preferably phenyl, phenylene, or benzene triyl, i.e., may be unsubstituted, mono-substituted, or di-substituted.

Among the species that may constitute the substituents on the aryl ring of R^5 or R^6 are fluoro, chloro, bromo, methoxy, ethoxy, isopropoxy, trimethylammonium (preferably with an iodide or chloride counterion), methoxycarbonyl, ethoxycarbonyl, formyl, acetyl, propanoyl, (N)-hexyldimethylammonium, hexylenetrimethylammonium, tri(oxyethylene)iodide, and tetra(oxyethylene)trimethyl-ammonium iodide, each substituted at the p-position, the m-position, or both of the aryl ring. Other substituents that can be present on a phenylene, benzene triyl or other aromatic ring includes 3, 4-dioxymethylene (5-membered ring) and 3, 4-dioxyethylene (6-membered ring). One group of compounds of interest are those in which R^5 or R^6 is selected from phenyl, p-fluorophenyl, m-fluorophenyl, p-hydroxyphenyl, m-hydroxyphenyl, p-methoxyphenyl, m-methoxyphenyl, p-N,N-dimethylaminophenyl, m-N, N-dimethylaminophenyl, I$^-$ p-$(CH_3)_3$-N$^+$-phenyl, I$^-$ m-$(CH_3)_3$-N$^+$-phenyl, I$^-$ m-$(CH_3)_3$-N$^+$-CH_2CH_2-$(OCH_2CH_2)_2$-O-phenyl, I$^-$ p-$(CH_3)_3$-N$^+$-CH_2CH_2-$(OCH_2CH_2)_2$-O-phenyl, I$^-$ m-(N,N-dimethylpiperazinium)-(N')-CH_2-$(OCH_2CH_2)_2$-O-phenyl, 3-methoxy-4-fluorophenyl, thienyl-2-yl, 5-cholorothienyl-2-yl, 3, 4-difluorophenyl, I- p-(N,N-dimethylpiperazinium)-(N')-CH_2-$OCH_2CH_2)_2$-O-phenyl, 3-fluoro-4-methoxyphenyl, 4-pyridinyl, 2-pyridinyl, 3-pyridinyl, N-methyl-4-pyridinium,

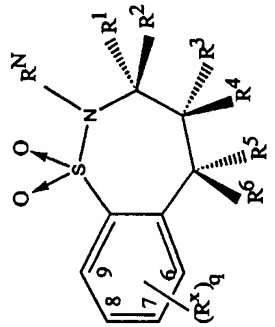
I⁻ N-methyl-3-pyridinium, 3, 4-dioxymethylenephenyl, 3, 4-dioxyethylenephenyl, and p-methoxycarbonylphenyl.

Preferred compounds include 3-ethyl-3-butyl and 3-butyl-3-butyl compounds having each of the above preferred R^5 substituents in combination with the R^x substituents shown in Tables 1, 2 and 3 below. It is particularly preferred that one, but not both, of R^5 and R^6 is hydrogen.

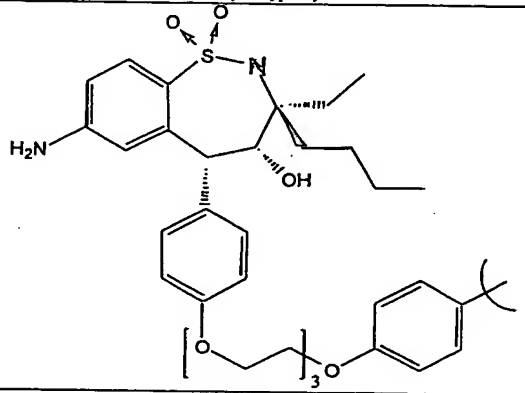
It is especially preferred that R^4 and R^6 be hydrogen, that R^3 and R^5 not be hydrogen, and that R^3 and R^5 be oriented in the same direction relative to the plane of the molecule, i.e., both in α- or both in β-configuration. It is further preferred that, where R^2 is butyl and R^1 is ethyl, then R^1 has the same orientation relative to the plane of the molecule as R^3 and R^5.

A class of compounds of particular interest comprises those 1,2-benzothiazepines wherein the R^1, R^2, R^3, R^4 and R^5 radicals are as set forth in Table 1 below; the R^6 radical is hydrogen; the R^N radical is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl and benzyl; and the R^x radical or radicals are independently selected from the group of R^x radicals disclosed in Table 1 below. The first part of Table 1 identifies the R^1, R^2, R^3, R^4 and R^5 radicals for each compound and the second part of Table 1 identifies the R^x radical or radicals for those compounds.

TABLE 1



Compound Number	R^1	R^2	R^3	R^4	R^5
101	ethyl	n-butyl	OH	H	phenyl
102	ethyl	n-butyl	OH	H	phenyl
103	n-butyl	ethyl	OH	H	phenyl
104	ethyl	n-butyl	OH	H	phenyl
105	ethyl	n-butyl	OH	H	phenyl
106	ethyl	n-butyl	OH	H	4-(decyloxy)phenyl
107	n-butyl	ethyl	OH	H	phenyl
108	ethyl	n-butyl	OH	H	4-(decyloxy)phenyl
109	ethyl	n-butyl	OH	H	

110	ethyl	n-butyl	OH	H	phenyl
111	n-butyl	ethyl	OH	H	4-hydroxyphenyl
112	ethyl	n-butyl	OH	H	
113	ethyl	n-butyl	OH	H	4-hydroxyphenyl
114	ethyl	n-butyl	OH	H	4-methoxyphenyl
115	n-butyl	ethyl	OH	H	4-methoxyphenyl
116	ethyl	n-butyl	OH	H	4-methoxyphenyl
117	n-butyl	ethyl	OH	H	phenyl
118	ethyl	n-butyl	OH	H	phenyl
119	ethyl	n-butyl	OH	H	phenyl
120	n-butyl	ethyl	OH	H	phenyl
121	ethyl	n-butyl	OH	H	phenyl
122	n-butyl	ethyl	OH	H	phenyl
123	ethyl	n-butyl	OH	H	phenyl

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124	n-butyl	ethyl	OH	H	phenyl
125	ethyl	n-butyl	OH	H	phenyl
126	n-butyl	ethyl	OH	H	4-fluorophenyl
127	n-butyl	ethyl	OH	H	4-fluorophenyl
128	ethyl	n-butyl	OH	H	4-fluorophenyl
129	ethyl	n-butyl	OH	H	4-fluorophenyl
131	ethyl	n-butyl	OH	H	4-fluorophenyl
132	ethyl	n-butyl	OH	H	phenyl
133	ethyl	n-butyl	OH	H	phenyl
134	ethyl	n-butyl	OH	H	phenyl
135	ethyl	n-butyl	OH	H	phenyl
136	ethyl	n-butyl	OH	H	phenyl
137	n-butyl	ethyl	OH	H	phenyl
138	n-butyl	ethyl	OH	H	phenyl
139	n-butyl	ethyl	OH	H	Phenyl
142	ethyl	n-butyl	H	OH	H
143	ethyl	n-butyl	OH	H	3-methoxyphenyl
144	ethyl	n-butyl	OH	H	4-fluorophenyl
262	ethyl	n-butyl	OH	H	3-methoxyphenyl
263	ethyl	n-butyl	H	OH	H
264	ethyl	n-butyl	OH	H	3-trifluoromethylphenyl
265	ethyl	n-butyl	H	OH	H
266	ethyl	n-butyl	OH	H	3-hydroxyphenyl
267	ethyl	n-butyl	OH	H	3-hydroxyphenyl
268	ethyl	n-butyl	OH	H	4-fluorophenyl
269	ethyl	n-butyl	H	OH	H
270	ethyl	n-butyl	OH	H	4-fluorophenyl
271	ethyl	n-butyl	OH	H	3-methoxyphenyl
272	ethyl	n-butyl	H	OH	H
273	ethyl	n-butyl	H	OH	H
274	ethyl	n-butyl	OH	H	4-fluorophenyl
275	ethyl	n-butyl	H	OH	H
276	ethyl	n-butyl	OH	H	3-methoxyphenyl

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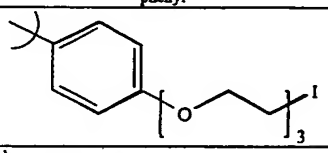
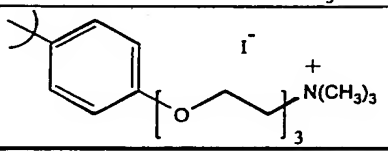
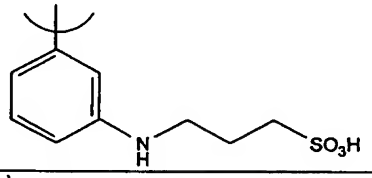
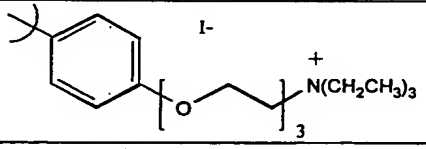
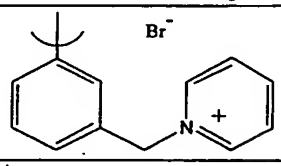
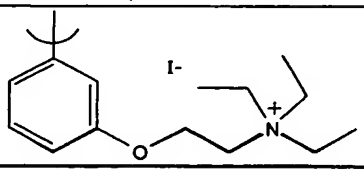
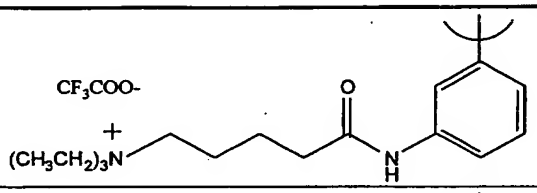
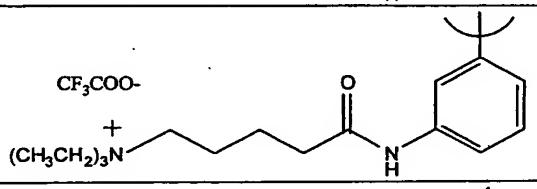
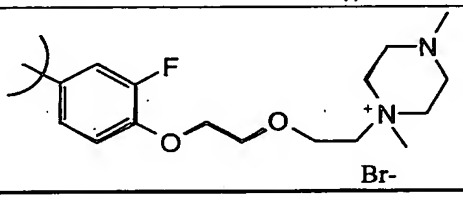
277	ethyl	n-butyl	OH	H	3-fluorophenyl
278	ethyl	n-butyl	H	OH	2-fluorophenyl
279	ethyl	n-butyl	H	OH	3-fluorophenyl
280	ethyl	n-butyl	OH	H	2-fluorophenyl
281	ethyl	n-butyl	OH	H	4-fluorophenyl
282	ethyl	n-butyl	OH	H	4-fluorophenyl
283	ethyl	n-butyl	H	OH	H
284	ethyl	n-butyl	OH	H	4-fluorophenyl
286	ethyl	ethyl	OH	H	phenyl
287	ethyl	ethyl	OH	H	phenyl
288	methyl	methyl	OH	H	phenyl
289	n-butyl	n-butyl	OH	H	phenyl
290	n-butyl	n-butyl	OH	H	phenyl
291	n-butyl	n-butyl	OH	H	phenyl
292	n-butyl	n-butyl	OH	H	4-fluorophenyl
293	n-butyl	n-butyl	OH	H	phenyl
294	n-butyl	n-butyl	OH	H	phenyl
295	ethyl	n-butyl	OH	H	
296	ethyl	n-butyl	OH	H	

1000	ethyl	n-butyl	OH	H	
1001	ethyl	n-butyl	OH	H	
1002	ethyl	n-butyl	OH	H	
1003	ethyl	n-butyl	OH	H	

1004	ethyl	n-butyl	OH	H	
1005	n-butyl	n-butyl	OH	H	
1006	n-butyl	n-butyl	OH	H	

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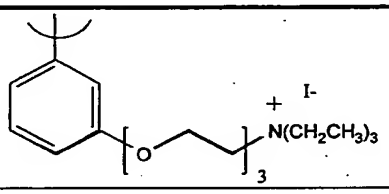
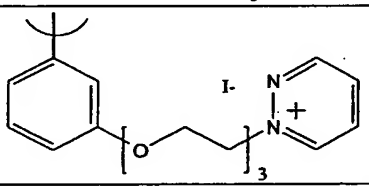
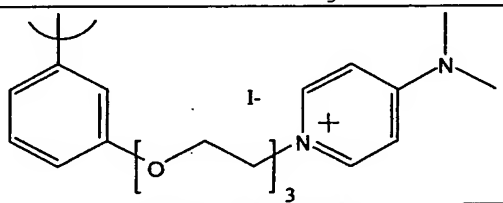
1007	n-butyl	n-butyl	OH	H	
1008	n-butyl	n-butyl	OH	H	
1009	n-butyl	n-butyl	OH	H	
1010	n-butyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1011	n-butyl	n-butyl	OH	H	3-fluoro-4-(5-triethylammoniumpentyloxy)phenyl, trifluoroacetate salt
1012	n-butyl	n-butyl	OH	H	4-hydroxyphenyl

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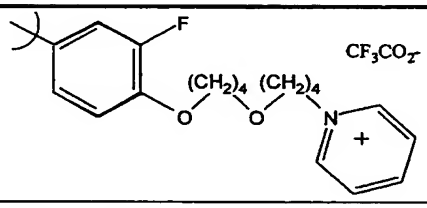
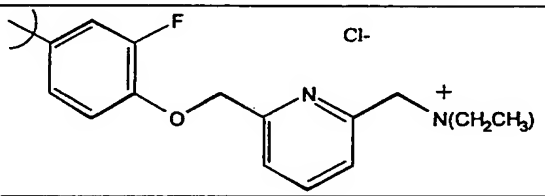
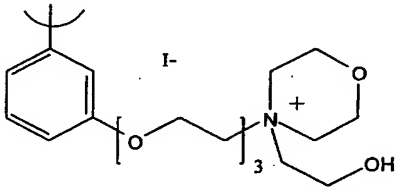
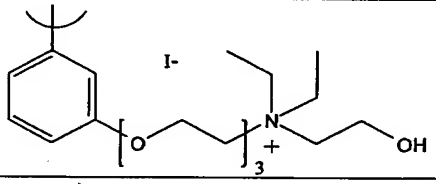
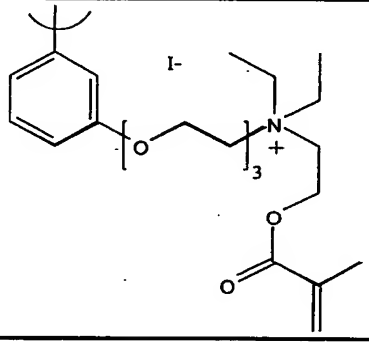
1013	n-butyl	n-butyl	OH	H	
1014	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1015	n-butyl	n-butyl	OH	H	
1016	n-butyl	n-butyl	OH	H	

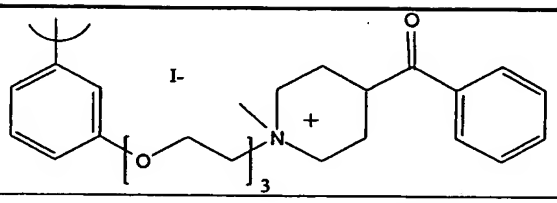
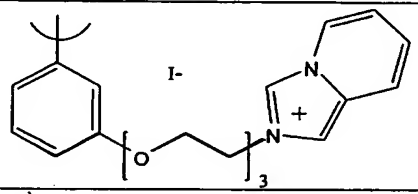
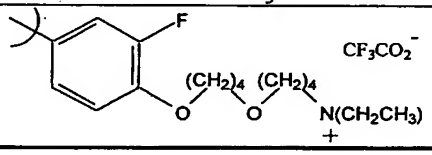
1017	n-butyl	n-butyl	OH	H	
1018	n-butyl	n-butyl	OH	H	

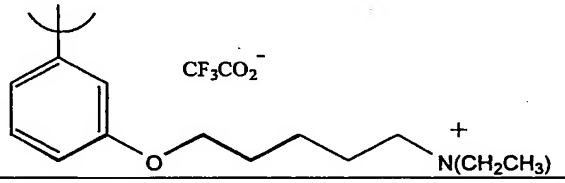
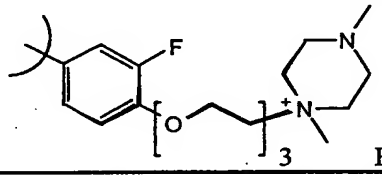
1019	n-butyl	n-butyl	OH	H	
1020	n-butyl	n-butyl	OH	H	
1021	n-butyl	n-butyl	OH	H	

1022	n-butyl	n-butyl	OH	H	
1023	n-butyl	n-butyl	OH	H	

1024	n-butyl	n-butyl	OH	H	
1025	n-butyl	n-butyl	OH	H	

1026	n-butyl	n-butyl	OH	H	
1027	n-butyl	n-butyl	OH	H	
1028	n-butyl	n-butyl	OH	H	

1029	n-butyl	n-butyl	OH	H	
1030	n-butyl	n-butyl	OH	H	
1031	n-butyl	n-butyl	OH	H	

1032	n-butyl	n-butyl	OH	H	
1033	n-butyl	n-butyl	OH	H	

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1034	n-butyl	n-butyl	OH	H	

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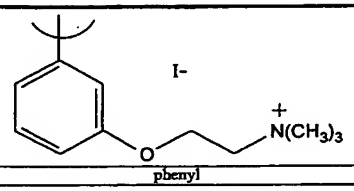
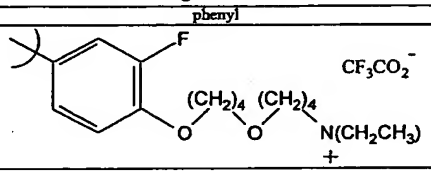
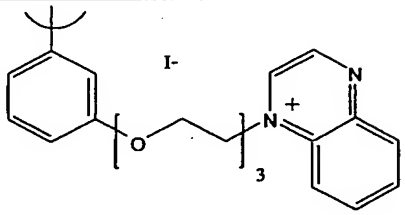
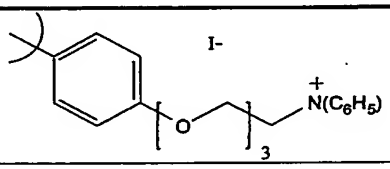
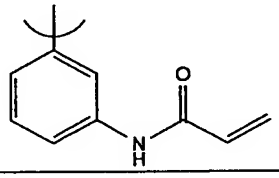
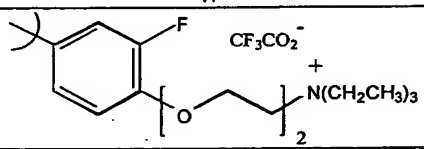
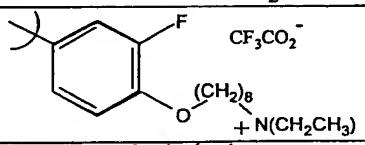
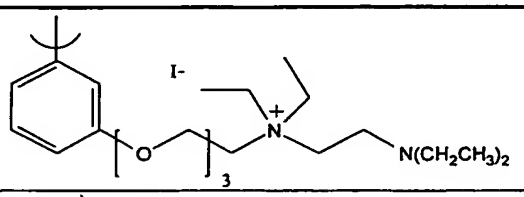
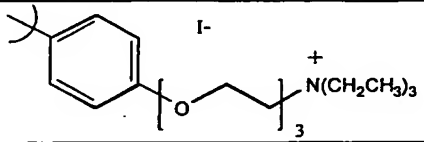
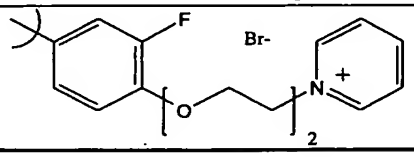
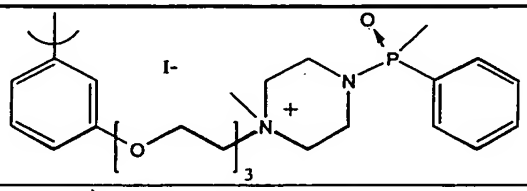
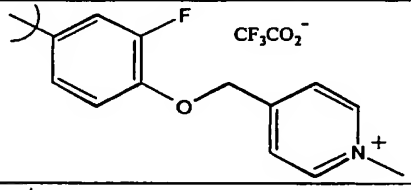
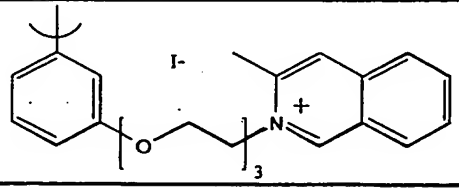
1035	n-butyl	n-butyl	OH	H	
1036	n-butyl	n-butyl	OH	H	
1037	n-butyl	n-butyl	OH	H	4-hydroxybenzyl

1038	n-butyl	n-butyl	OH	H	
1039	n-butyl	n-butyl	OH	H	phenyl
1040	n-butyl	n-butyl	OH	H	
1041	n-butyl	n-butyl	OH	H	

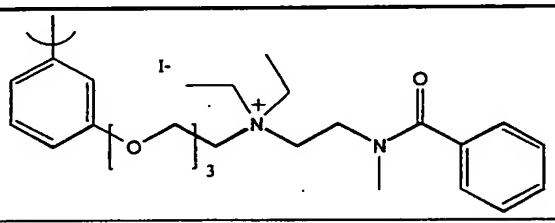
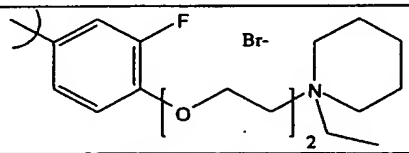
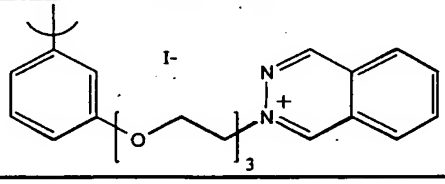
1042	n-butyl	n-butyl	OH	H	
1043	n-butyl	n-butyl	OH	H	
1044	n-butyl	n-butyl	OH	H	
1045	n-butyl	n-butyl	OH	H	
1046	n-butyl	n-butyl	OH	H	3-aminophenyl

1047	n-butyl	n-butyl	OH	H	
1048	n-butyl	n-butyl	OH	H	
1049	n-butyl	n-butyl	OH	H	

1050	n-butyl	n-butyl	OH	H	
1051	n-butyl	n-butyl	OH	H	
1052	n-butyl	n-butyl	OH	H	

1053	n-butyl	n-butyl	OH	H	
1054	n-butyl	n-butyl	OH	H	

1055	n-butyl	n-butyl	OH	H	
1056	n-butyl	n-butyl	OH	H	
1057	n-butyl	n-butyl	OH	H	

1058	n-butyl	n-butyl	OH	H	
1059	n-butyl	n-butyl	OH	H	
1060	ethyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1061	n-butyl	n-butyl	OH	H	

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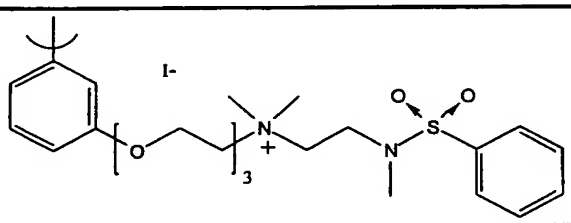
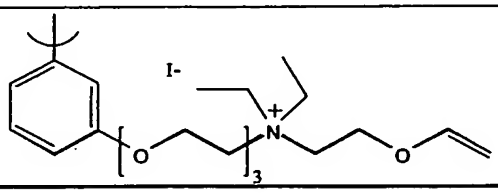
1062	n-butyl	n-butyl	OH	H	
1063	n-butyl	n-butyl	OH	H	

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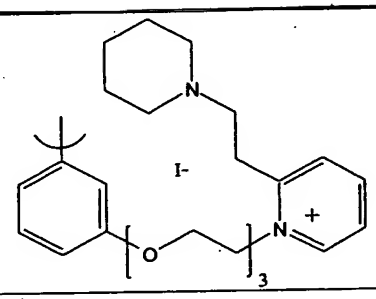
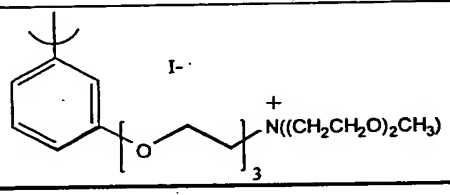
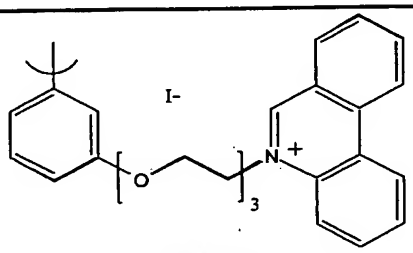
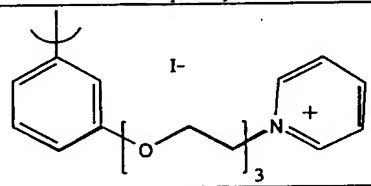
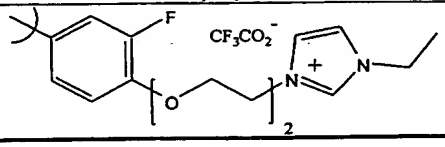
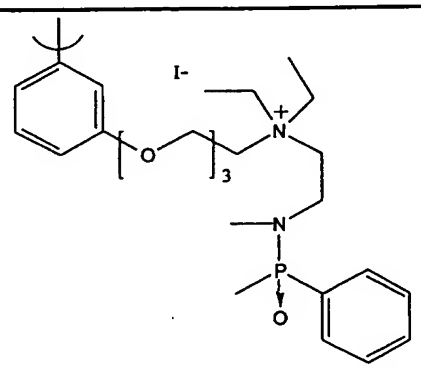
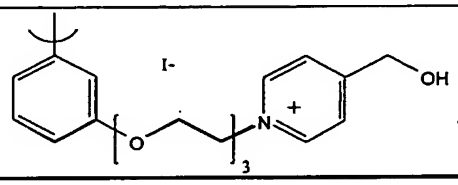
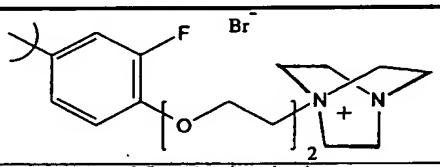
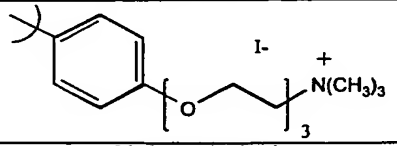
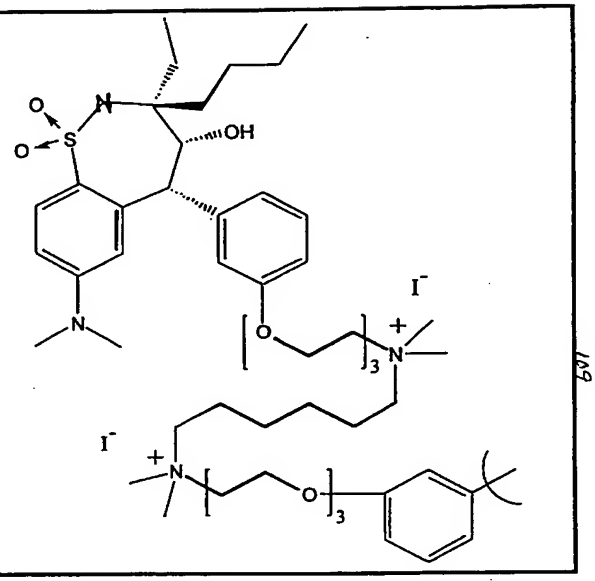
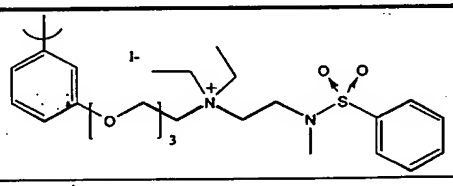
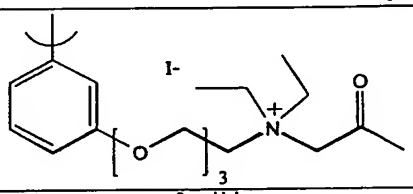
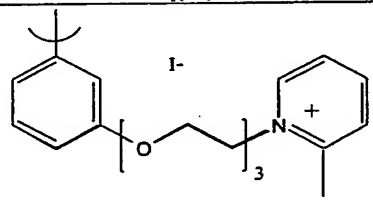
1064	n-butyl	n-butyl	OH	H	
1065	n-butyl	n-butyl	OH	H	

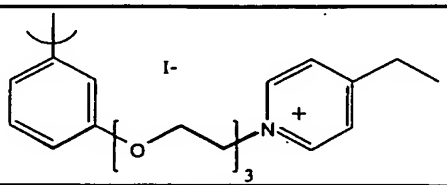
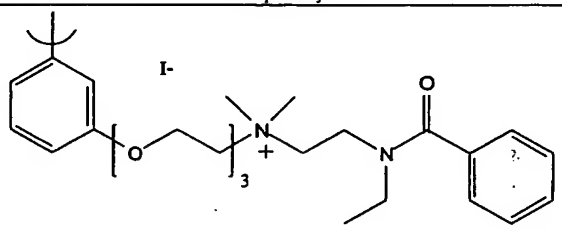
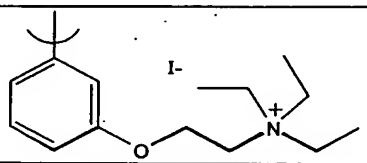
1066	n-butyl	n-butyl	OH	H	
1067	n-butyl	n-butyl	OH	H	thiophen-3-yl
1068	n-butyl	n-butyl	OH	H	
1069	n-butyl	n-butyl	OH	H	phenyl
1070	n-butyl	n-butyl	OH	H	

1071	n-butyl	n-butyl	OH	H	
1072	n-butyl	n-butyl	OH	H	

1073	n-butyl	n-butyl	OH	H	
1074	ethyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1075	n-butyl	n-butyl	OH	H	4-fluorophenyl
1076	n-butyl	n-butyl	OH	H	
1077	n-butyl	n-butyl	OH	H	3-hydroxymethylphenyl
1078	ethyl	n-butyl	OH	H	4-hydroxyphenyl

1079	ethyl	n-butyl	OH	H	

1080	n-butyl	n-butyl	OH	H	
1081	n-butyl	n-butyl	OH	H	
1082	n-butyl	n-butyl	OH	H	2-pyridyl
1083	n-butyl	n-butyl	OH	H	

1084	n-butyl	n-butyl	OH	H	
1085	n-butyl	n-butyl	OH	H	thiophen-3-yl
1086	n-butyl	n-butyl	OH	H	
1087	n-butyl	n-butyl	OH	H	
1088	ethyl	n-butyl	OH	H	3,4-methylenedioxyphenyl
1089	ethyl	n-butyl	OH	H	4-methoxyphenyl

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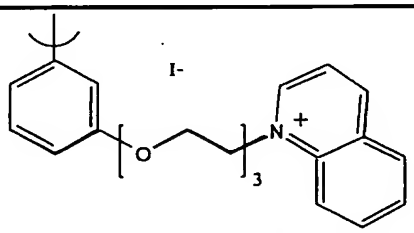
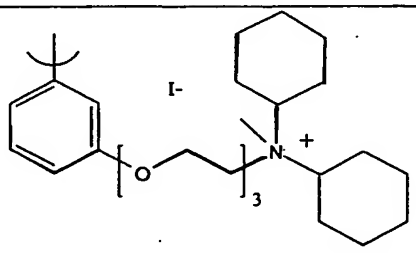
1090	n-butyl	n-butyl	OH	H	
1091	n-butyl	n-butyl	OH	H	

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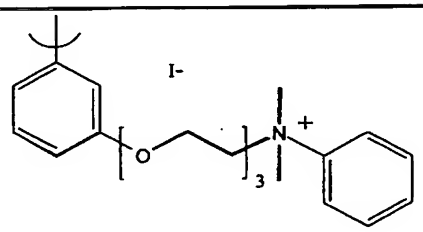
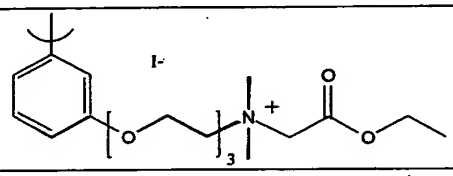
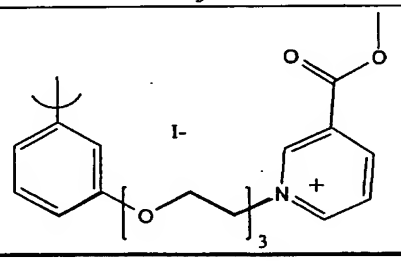
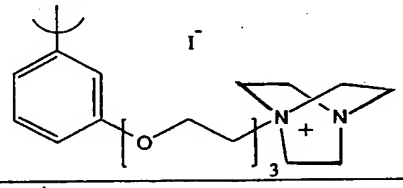
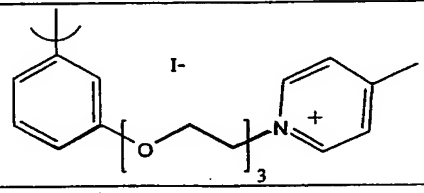
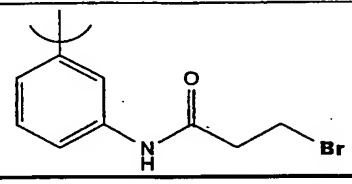
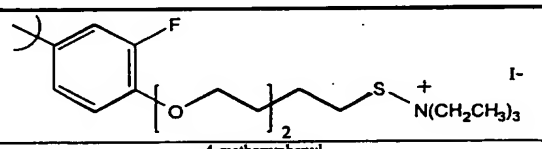
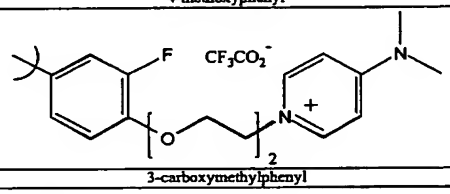
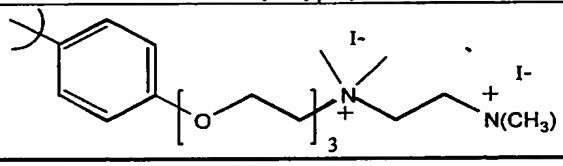
1092	n-butyl	n-butyl	OH	H	
1093	n-butyl	n-butyl	OH	H	
1094	n-butyl	n-butyl	OH	H	

1095	n-butyl	n-butyl	OH	H	
1096	n-butyl	n-butyl	OH	H	
1097	n-butyl	n-butyl	OH	H	

1098	n-butyl	n-butyl	OH	H	
1099	ethyl	n-butyl	OH	H	4-methoxyphenyl
1100	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1101	n-butyl	n-butyl	OH	H	
1102	n-butyl	n-butyl	OH	H	3-carboxymethylphenyl
1103	n-butyl	n-butyl	OH	H	

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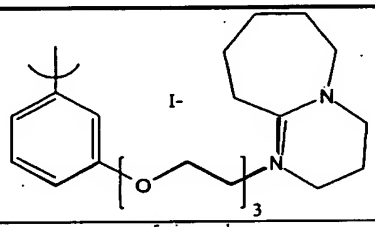
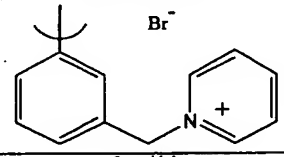
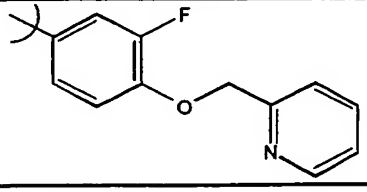
1104	n-butyl	n-butyl	OH	H	
1105	n-butyl	n-butyl	OH	H	5-piperonyl
1106	n-butyl	n-butyl	OH	H	3-hydroxyphenyl
1107	n-butyl	n-butyl	OH	H	
1108	n-butyl	n-butyl	OH	H	3-pyridyl
1109	n-butyl	n-butyl	OH	H	

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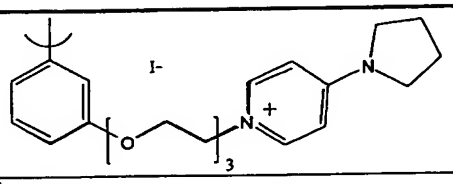
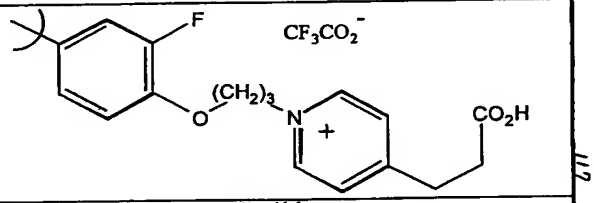
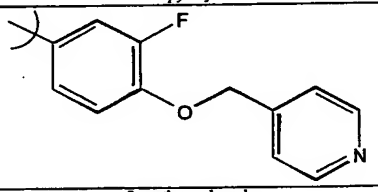
1110	n-butyl	n-butyl	OH	H	
1111	n-butyl	n-butyl	OH	H	
1112	n-butyl	n-butyl	OH	H	4-pyridyl
1113	n-butyl	n-butyl	OH	H	
1114	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1115	n-butyl	n-butyl	OH	H	4-fluorophenyl
1116	ethyl	n-butyl	OH	H	3-tolyl

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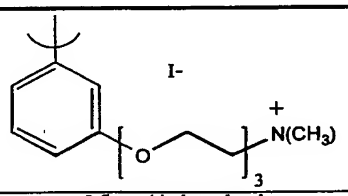
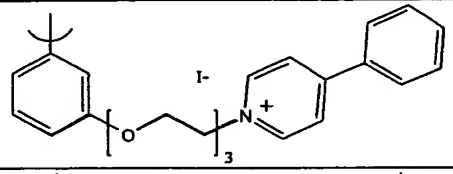
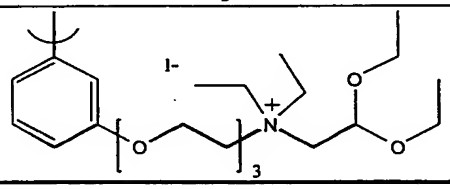
1117	ethyl	n-butyl	OH	H	
1118	ethyl	n-butyl	OH	H	3-fluoro-4-hydroxyphenyl
1119	n-butyl	n-butyl	OH	H	
1120	n-butyl	n-butyl	OH	H	

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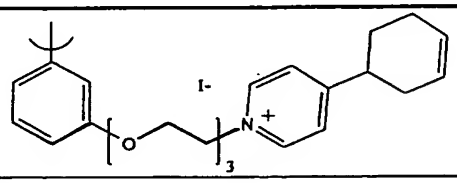
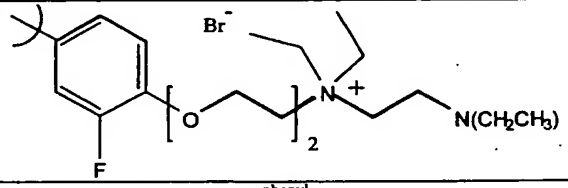
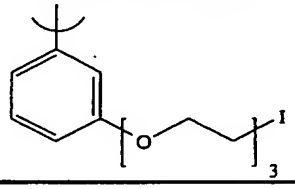
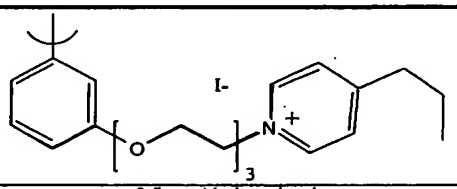
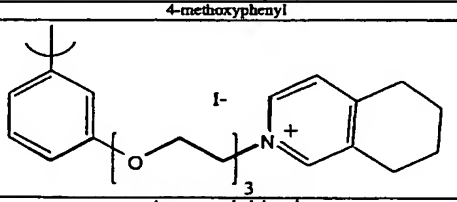
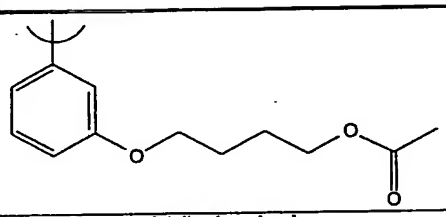
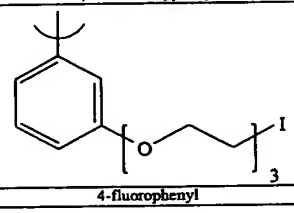
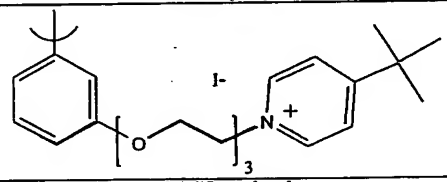
1121	n-butyl	n-butyl	OH	H	
1122	n-butyl	n-butyl	OH	H	
1123	n-butyl	n-butyl	OH	H	phenyl
1124	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1125	n-butyl	n-butyl	OH	H	3-chloro-4-methoxyphenyl
1126	ethyl	n-butyl	OH	H	

1127	n-butyl	n-butyl	OH	H	
1128	n-butyl	n-butyl	OH	H	3-fluoro-4-hydroxyphenyl
1129	n-butyl	n-butyl	OH	H	4-fluorophenyl
1130	n-butyl	n-butyl	OH	H	3-chloro-4-fluorophenyl
1131	ethyl	n-butyl	OH	H	4-methoxyphenyl
1132	n-butyl	n-butyl	OH	H	
1133	n-butyl	n-butyl	OH	H	4-cyanomethylphenyl

1134	ethyl	n-butyl	OH	H	
1135	n-butyl	n-butyl	OH	H	3,4-dimethoxyphenyl
1136	n-butyl	n-butyl	OH	H	
1137	n-butyl	n-butyl	OH	H	4-fluorophenyl
1138	n-butyl	n-butyl	OH	H	
1139	n-butyl	n-butyl	OH	H	3,4-difluorophenyl
1140	n-butyl	n-butyl	OH	H	3-methoxyphenyl

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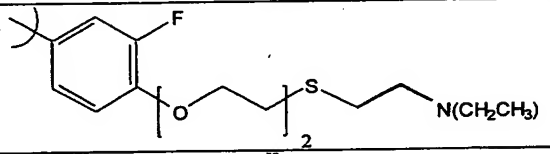
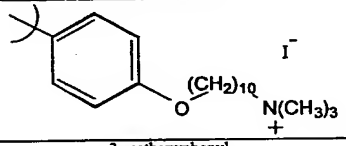
1141	n-butyl	n-butyl	OH	H	4-fluorophenyl
1142	n-butyl	n-butyl	OH	H	
1143	n-butyl	n-butyl	H	OH	H
1144	n-butyl	n-butyl	OH	H	5-piperonyl
1145	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1146	n-butyl	n-butyl	OH	H	
1147	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1148	n-butyl	n-butyl	OH	H	4-fluorophenyl
1149	n-butyl	n-butyl	OH	H	4-fluorophenyl
1150	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1151	n-butyl	ethyl	OH	H	3-fluoro-4-methoxyphenyl
1152	n-butyl	n-butyl	OH	H	phenyl
1153	n-butyl	n-butyl	OH	H	4-fluorophenyl
1154	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1155	n-butyl	n-butyl	OH	H	4-fluorophenyl
1156	n-butyl	n-butyl	OH	H	4-fluorophenyl
1157	n-butyl	n-butyl	OH	H	4-fluorophenyl
1158	n-butyl	n-butyl	OH	H	4-pyridinyl, hydrochloride salt
1159	n-butyl	ethyl	OH	H	phenyl
1160	n-butyl	n-butyl	OH	H	4-fluorophenyl

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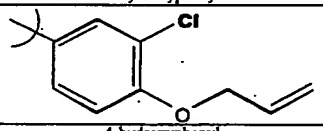
1161	n-butyl	n-butyl	OH	H	3,5-dichloro-4-methoxyphenyl
1162	n-butyl	n-butyl	OH	H	phenyl
1163	n-butyl	n-butyl	OH	H	3-(dimethylamino)phenyl
1164	n-butyl	n-butyl	OH	H	4-pyridinyl
1165	n-butyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1166	n-butyl	n-butyl	OH	H	3-hydroxyphenyl
1167	n-butyl	n-butyl	OH	H	
1168	n-butyl	n-butyl	OH	H	4-hydroxyphenyl
1169	n-butyl	n-butyl	OH	H	phenyl
1170	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1171	n-butyl	n-butyl	OH	H	4-(trifluoromethylsulfonyloxy)phenyl
1172	n-butyl	n-butyl	OH	H	4-pyridinyl
1173	n-butyl	n-butyl	OH	H	4-fluorophenyl
1174	ethyl	n-butyl	OH	H	3-methoxyphenyl
1175	ethyl	n-butyl	OH	H	3-methoxyphenyl
1176	n-butyl	n-butyl	OH	H	4-fluorophenyl
1177	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1178	n-butyl	n-butyl	OH	H	3-(trifluoromethylsulfonyloxy)phenyl
1179	n-butyl	n-butyl	OH	H	phenyl
1180	n-butyl	n-butyl	OH	H	phenyl
1181	n-butyl	n-butyl	OH	H	4-fluorophenyl
1182	n-butyl	n-butyl	OH	H	4-(dimethylamino)phenyl
1183	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1184	n-butyl	n-butyl	OH	H	4-fluorophenyl
1185	n-butyl	n-butyl	OH	H	4-fluorophenyl
1186	n-butyl	n-butyl	OH	H	phenyl
1187	n-butyl	n-butyl	OH	H	4-fluorophenyl
1188	n-butyl	n-butyl	OH	H	4-methoxyphenyl

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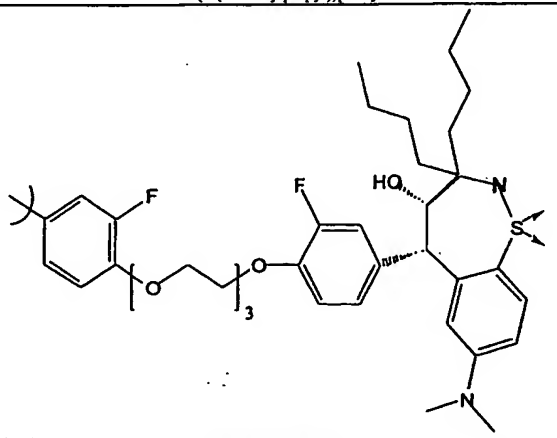
1189	n-butyl	n-butyl	OH	H	3,4-difluorophenyl
1190	n-butyl	n-butyl	OH	H	2-bromophenyl
1191	n-butyl	n-butyl	OH	H	4-(dimethylamino)phenyl
1192	n-butyl	n-butyl	OH	H	3-(dimethylamino)phenyl
1193	n-butyl	n-butyl	OH	H	4-(2-(2-methylpropyl))phenyl
1194	n-butyl	n-butyl	OH	H	
1195	n-butyl	n-butyl	OH	H	4-methoxyphenyl

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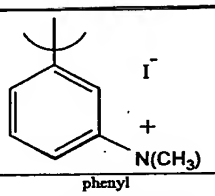
1196	n-butyl	n-butyl	OH	H	
1197	n-butyl	ethyl	R3 + R4 = oxo	R3 + R4 = oxo	phenyl
1198	n-butyl	n-butyl	OH	H	4-(pyridinyl-N-oxide)

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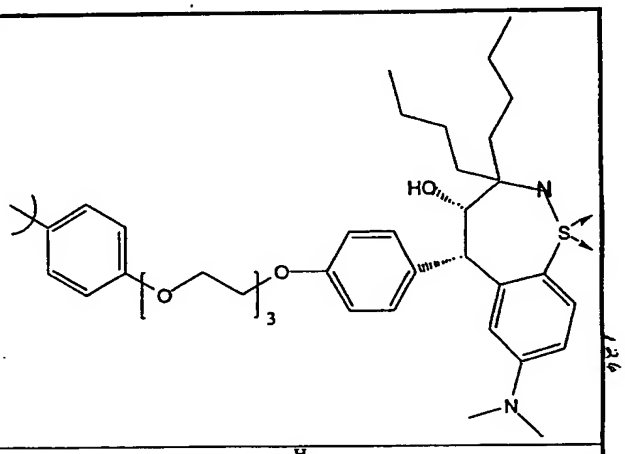
1199	n-butyl	n-butyl	OH	H	
1200	n-butyl	n-butyl	H	OH	H
1201	n-butyl	n-butyl	OH	H	H

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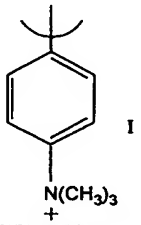
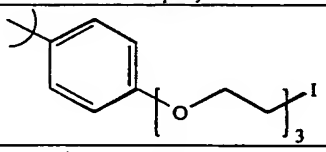
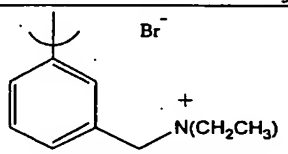
1202	n-butyl	n-butyl	OH	H	
1203	n-butyl	n-butyl	OH	H	5-piperazinyl
1204	n-butyl	n-butyl	OH	H	4-fluorophenyl
1205	n-butyl	n-butyl	OH	H	
1206	n-butyl	n-butyl	OH	H	
1207	n-butyl	n-butyl	OH	H	3,5-dichlorophenyl
1208	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1209	n-butyl	n-butyl	acetoxy	H	phenyl
1210	n-butyl	n-butyl	OH	H	2-(dimethylamino)phenyl

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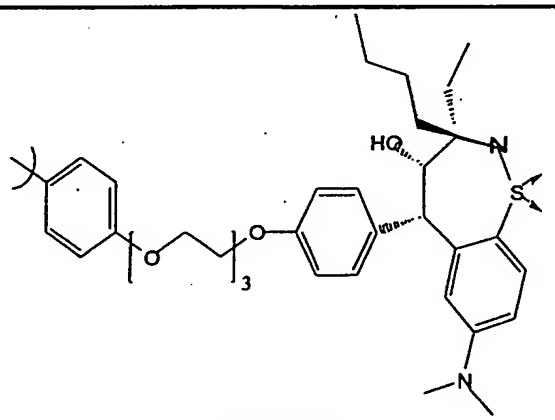
1211	ethyl	n-butyl	OH	H	
1212	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1213	n-butyl	ethyl	H	OH	H
1214	n-butyl	ethyl	OH	H	phenyl
1215	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1216	ethyl	n-butyl	OH	H	5-piperonyl
1217	n-butyl	n-butyl	OH	H	4-carboxyphenyl
1218	n-butyl	n-butyl	OH	H	4-methoxyphenyl

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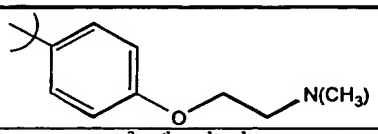
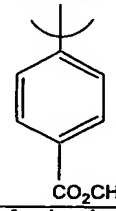
1219	n-butyl	n-butyl	OH	H	
1220	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1221	n-butyl	n-butyl	OH	H	
1222	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1223	n-butyl	n-butyl	OH	H	phenyl
1224	n-butyl	n-butyl	OH	H	3-nitrophenyl
1225	n-butyl	ethyl	OH	H	3-methylphenyl
1226	ethyl	n-butyl	OH	H	5-piperonyl
1227	n-butyl	n-butyl	OH	H	4-fluorophenyl
1228	n-butyl	n-butyl	OH	H	2-pyrrolyl
1229	n-butyl	n-butyl	OH	H	3-chloro-4-hydroxyphenyl
1230	n-butyl	n-butyl	OH	H	phenyl

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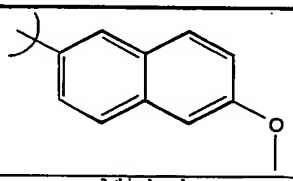
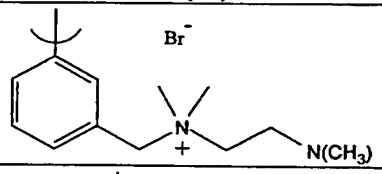
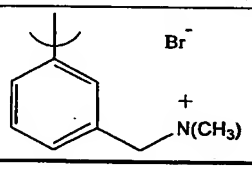
1231	n-butyl	n-butyl	OH	H	
1232	n-butyl	n-butyl	H	OH	3-thiophenyl
1233	n-butyl	n-butyl	OH	H	
1234	n-butyl	n-butyl	OH	H	

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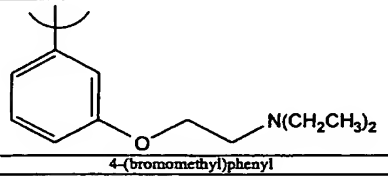
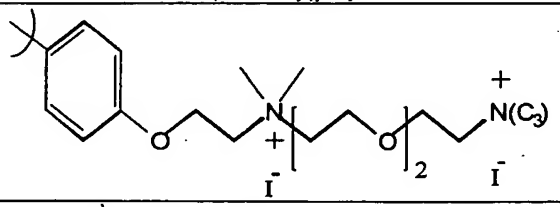
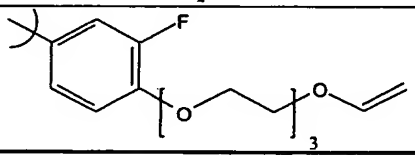
1235	n-butyl	n-butyl	OH	H	
1236	n-butyl	n-butyl	OH	H	4-(bromomethyl)phenyl
1237	n-butyl	n-butyl	OH	H	
1238	n-butyl	n-butyl	OH	H	

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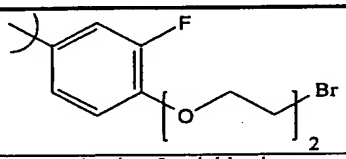
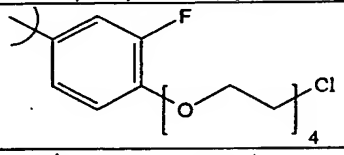
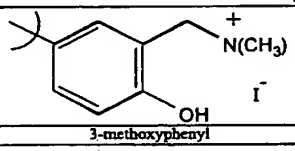
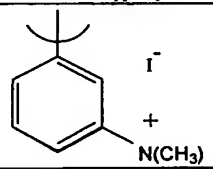
1239	n-butyl	n-butyl	OH	H	
1240	n-butyl	n-butyl	OH	H	4-methoxy-3-methylphenyl
1241	n-butyl	n-butyl	OH	H	3-(dimethylaminomethyl)phenyl
1242	n-butyl	n-butyl	OH	H	
1243	n-butyl	n-butyl	OH	H	
1244	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1245	n-butyl	n-butyl	OH	H	

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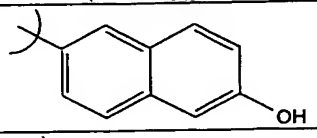
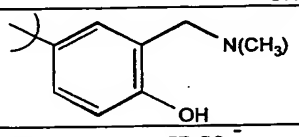
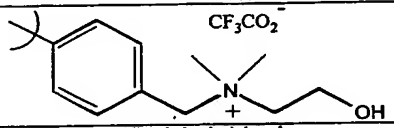
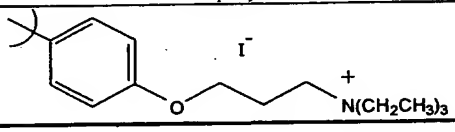
1246	n-butyl	n-butyl	OH	H	3-(bromomethyl)phenyl
1247	n-butyl	n-butyl	OH	H	
1248	n-butyl	n-butyl	OH	H	
1249	n-butyl	n-butyl	OH	H	
1250	n-butyl	n-butyl	OH	H	3-(dimethylamino)phenyl
1251	n-butyl	n-butyl	OH	H	1-naphthyl
1252	n-butyl	n-butyl	OH	H	

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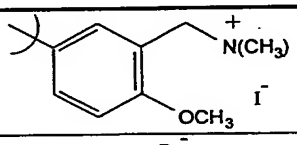
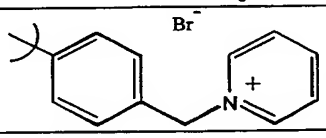
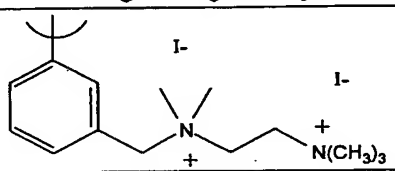
1253	n-butyl	n-butyl	OH	H	
1254	n-butyl	n-butyl	OH	H	
1255	n-butyl	n-butyl	OH	H	
1256	n-butyl	n-butyl	OH	H	3-nitrophenyl
1257	n-butyl	n-butyl	OH	H	phenyl
1258	n-butyl	n-butyl	OH	H	4-fluorophenyl
1259	ethyl	n-butyl	H	OH	H
1260	ethyl	n-butyl	OH	H	3-hydroxyphenyl

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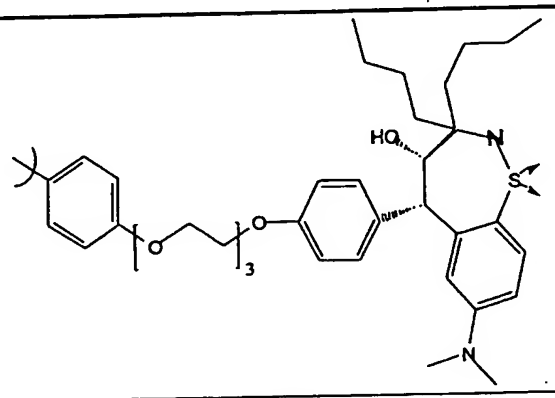
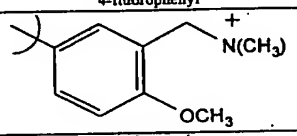
1261	n-butyl	n-butyl	OH	H	
1262	n-butyl	n-butyl	OH	H	2-thiophenyl
1263	n-butyl	n-butyl	OH	H	5-piperonyl
1264	n-butyl	n-butyl	OH	H	4-fluorophenyl
1265	n-butyl	n-butyl	OH	H	4-fluorophenyl
1266	n-butyl	n-butyl	OH	H	
1267	n-butyl	ethyl	OH	H	5-piperonyl

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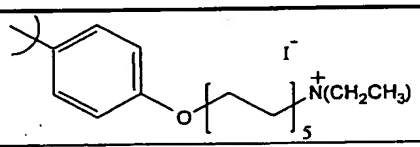
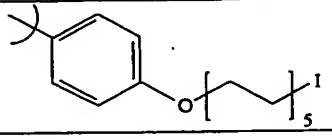
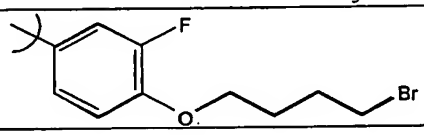
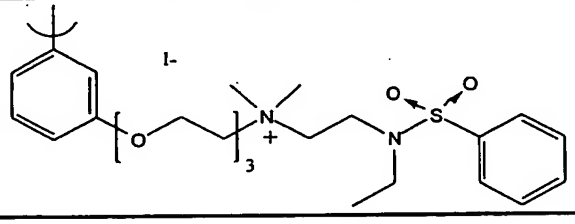
1268	n-butyl	n-butyl	OH	H	
1269	n-butyl	n-butyl	OH	H	
1270	n-butyl	n-butyl	OH	H	
1271	n-butyl	n-butyl	OH	H	

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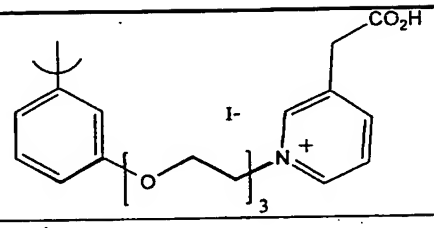
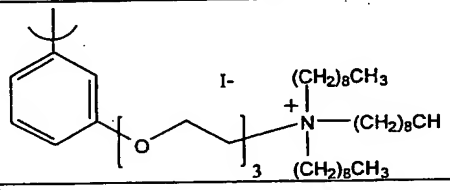
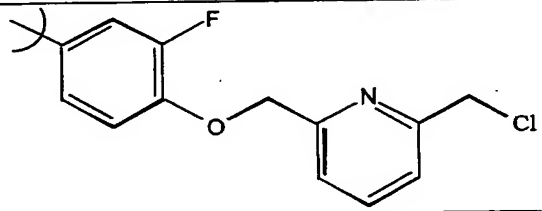
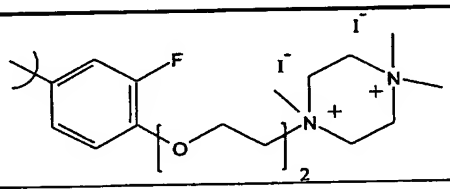
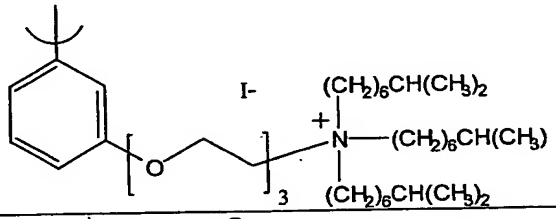
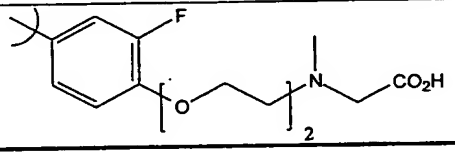
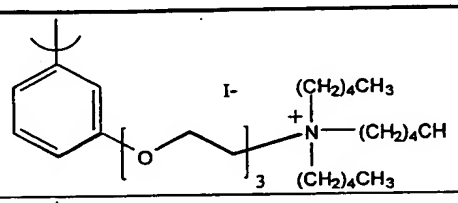
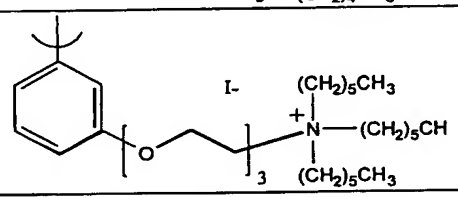
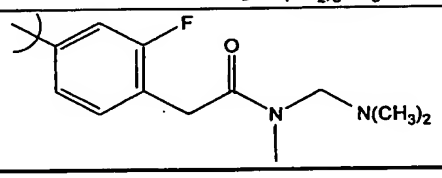
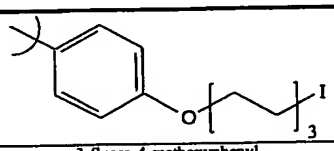
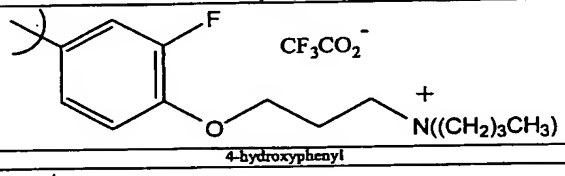
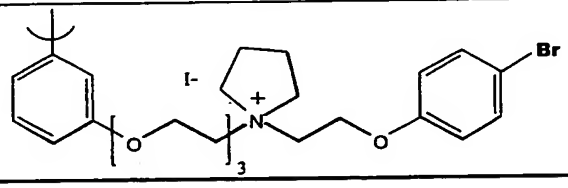
1272	n-butyl	n-butyl	OH	H	
1273	n-butyl	n-butyl	OH	H	
1274	n-butyl	n-butyl	OH	H	

1275	n-butyl	n-butyl	OH	H	
1276	n-butyl	n-butyl	OH	H	
1277	n-butyl	n-butyl	OH	H	

1278	n-butyl	n-butyl	OH	H	
1279	n-butyl	n-butyl	OH	H	
1280	n-butyl	n-butyl	OH	H	

1281	n-butyl	n-butyl	OH	H	
1282	ethyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1283	n-butyl	n-butyl	OH	H	4-hydroxymethylphenyl
1284	n-butyl	n-butyl	OH	H	4-fluorophenyl
1285	n-butyl	ethyl	OH	H	phenyl
1286	n-butyl	n-butyl	OH	H	
1287	n-butyl	ethyl	OH	H	4-hydroxyphenyl
1288	n-butyl	n-butyl	OH	H	

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1289	n-butyl	n-butyl	OH	H
1290	n-butyl	n-butyl	OH	H
1291	n-butyl	n-butyl	OH	H

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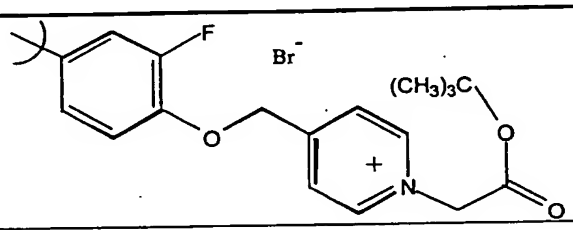
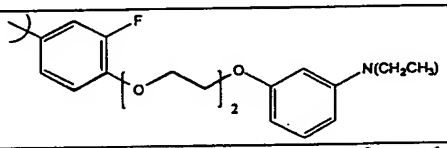
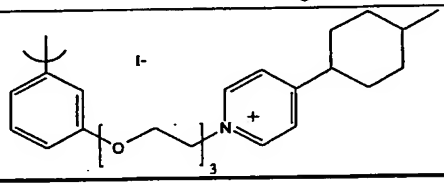
1292	n-butyl	n-butyl	OH	H
1293	n-butyl	n-butyl	OH	H
1294	n-butyl	n-butyl	OH	H

1295	n-butyl	n-butyl	OH	H	
1296	n-butyl	n-butyl	OH	H	
1297	n-butyl	n-butyl	OH	H	

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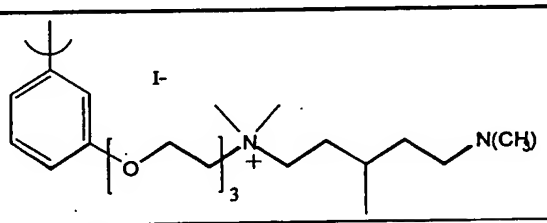
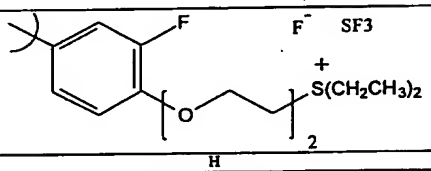
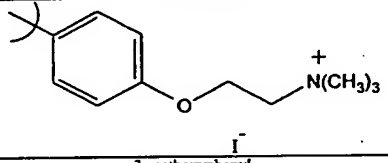
1298	n-butyl	n-butyl	OH	H	
1299	n-butyl	n-butyl	OH	H	
1300	n-butyl	ethyl	H	OH	H
1301	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1302	n-butyl	n-butyl	OH	H	3-hydroxyphenyl
1303	n-butyl	n-butyl	OH	H	
1304	n-butyl	n-butyl	OH	H	3-methoxyphenyl
1305	n-butyl	n-butyl	OH	H	4-fluorophenyl

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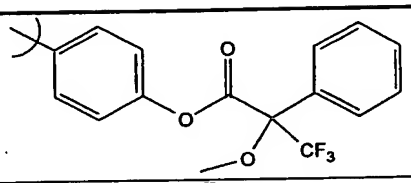
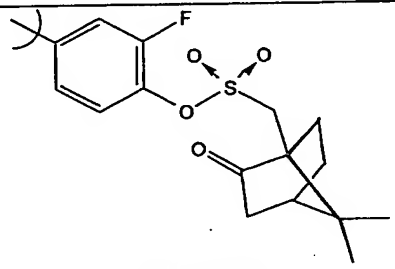
1306	n-butyl	n-butyl	OH	H	
1307	n-butyl	n-butyl	OH	H	H
1308	ethyl	n-butyl	OH	H	
1309	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1310	ethyl	n-butyl	OH	H	phenyl
1311	n-butyl	ethyl	OH	H	phenyl
1312	n-butyl	ethyl	OH	H	phenyl
1313	n-butyl	ethyl	OH	H	phenyl
1314	ethyl	n-butyl	OH	H	phenyl
1315	ethyl	n-butyl	OH	H	phenyl
1316	n-butyl	ethyl	OH	H	phenyl
1317	n-butyl	ethyl	OH	H	phenyl

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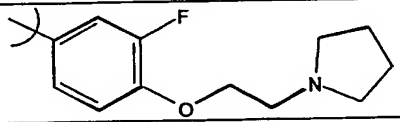
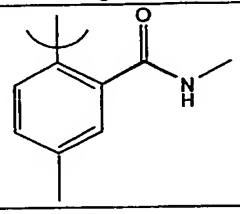
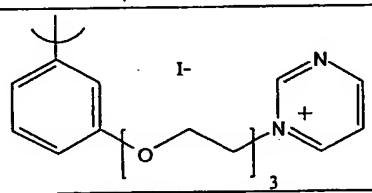
1318	ethyl	n-butyl	OH	H	phenyl
1319	ethyl	n-butyl	OH	H	3-methoxyphenyl
1320	ethyl	n-butyl	OH	H	phenyl
1321	n-butyl	ethyl	OH	H	phenyl
1322	n-butyl	n-butyl	OH	H	
1323	n-butyl	n-butyl	OH	H	
1324	n-butyl	n-butyl	OH	H	
1325	n-butyl	n-butyl	OH	H	4-((diethylamino)methyl)phenyl

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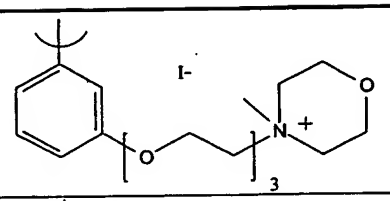
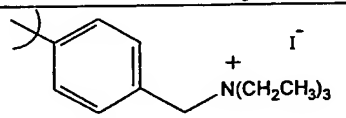
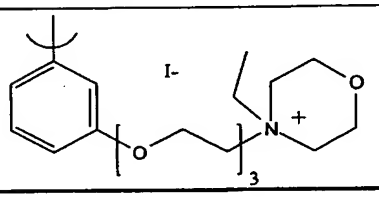
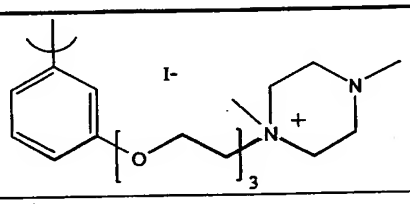
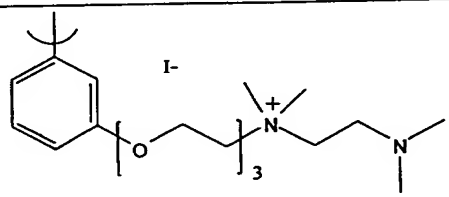
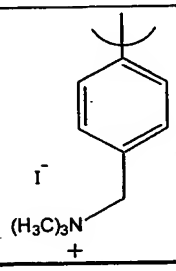
1326	n-butyl	n-butyl	OH	H	
1327	n-butyl	n-butyl	OH	H	3-fluoro-4-hydroxy-5-iodophenyl
1328	n-butyl	n-butyl	OH	H	
1329	n-butyl	n-butyl	OH	H	

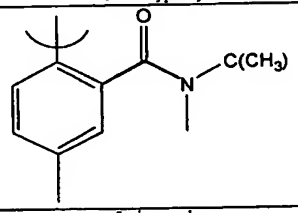
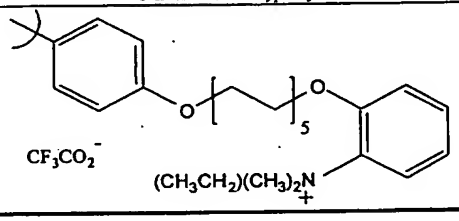
Fig. 14

1330	n-butyl	n-butyl	OH	H	
1331	n-butyl	n-butyl	OH	H	

Fig. 15

1332	n-butyl	n-butyl	OH	H	
1333	n-butyl	n-butyl	OH	H	
1334	n-butyl	n-butyl	OH	H	

1335	n-butyl	n-butyl	OH	H	
1336	n-butyl	n-butyl	OH	H	
1337	n-butyl	n-butyl	OH	H	

1338	n-butyl	n-butyl	OH	H	4-methoxyphenyl
1339	n-butyl	n-butyl	OH	H	
1340	n-butyl	ethyl	OH	H	5-piperonyl
1341	n-butyl	n-butyl	acetoxy	H	3-methoxyphenyl
1342	n-butyl	n-butyl	OH	H	5-piperonyl
1343	ethyl	n-butyl	OH	H	phenyl
1344	n-butyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1345	ethyl	n-butyl	OH	H	phenyl
1346	ethyl	n-butyl	OH	H	phenyl
1347	n-butyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1348	isobutyl	isobutyl	OH	H	phenyl
1349	ethyl	n-butyl	OH	H	phenyl
1350	n-butyl	n-butyl	OH	H	3-fluoro-4-methoxyphenyl
1351	n-butyl	n-butyl	OH	H	

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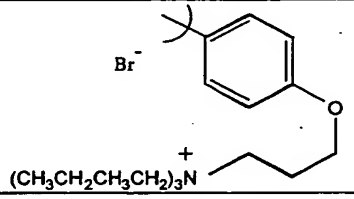
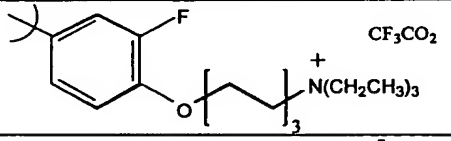
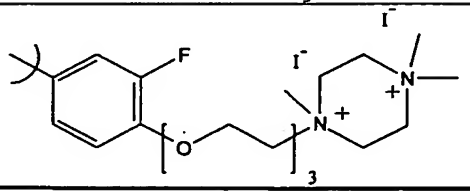
1352	n-butyl	n-butyl	OH	H	
1353	n-butyl	n-butyl	OH	H	
1354	n-butyl	n-butyl	OH	H	

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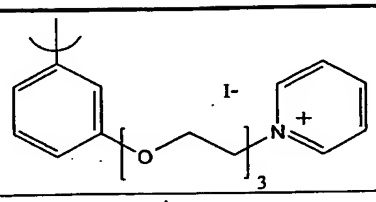
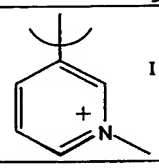
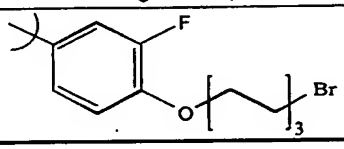
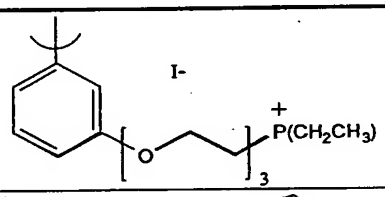
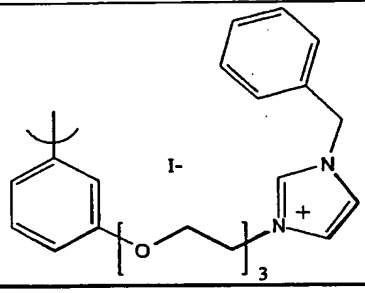
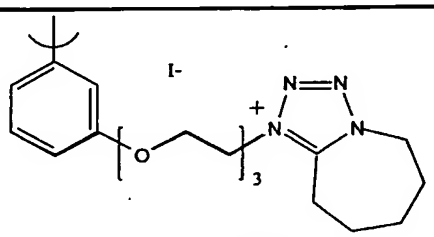
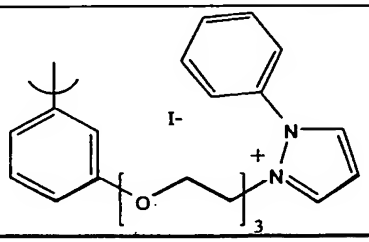
1355	n-butyl	n-butyl	OH	H	
1356	n-butyl	n-butyl	OH	H	
1357	n-butyl	n-butyl	OH	H	

1358	n-butyl	n-butyl	OH	H	
1359	n-butyl	n-butyl	OH	H	

1360	n-butyl	n-butyl	OH	H	
1361	n-butyl	n-butyl	OH	H	

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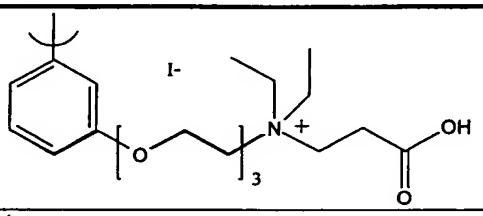
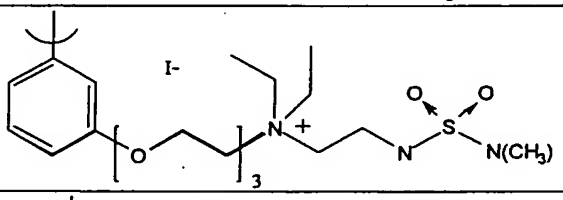
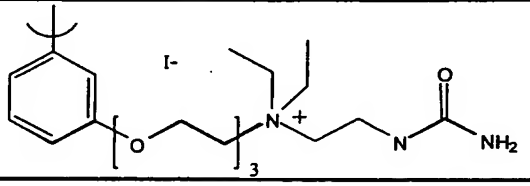
1362	n-butyl	n-butyl	OH	H	
1363	n-butyl	n-butyl	OH	H	
1364	n-butyl	n-butyl	OH	H	

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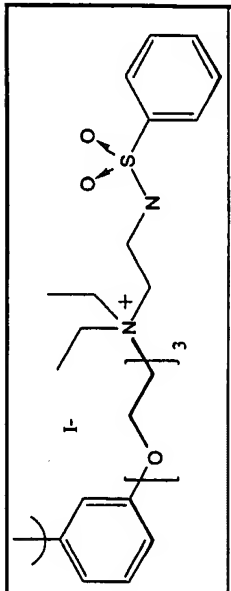
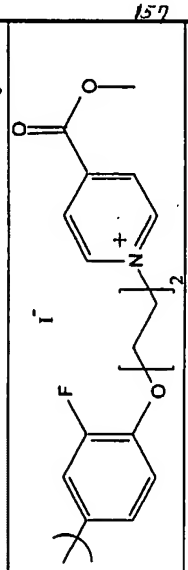
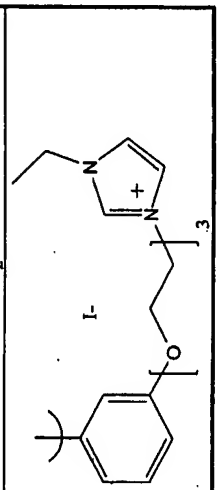
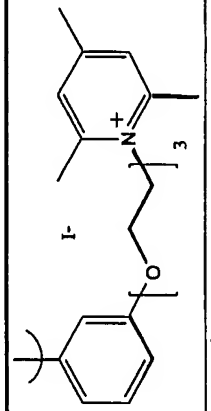
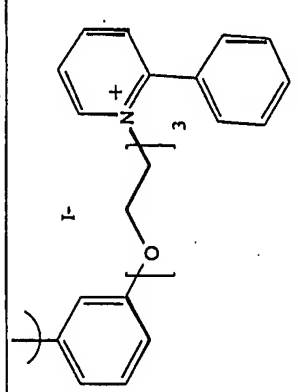
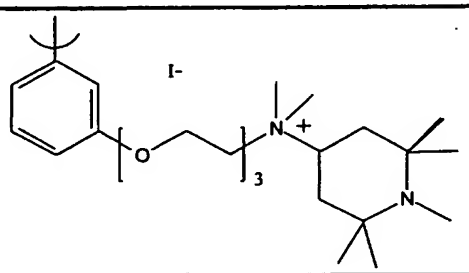
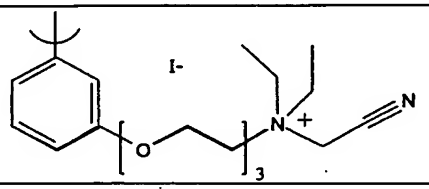
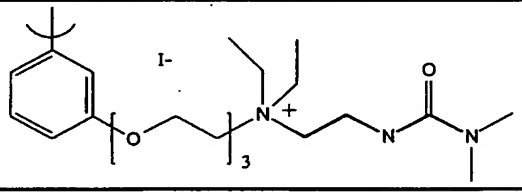
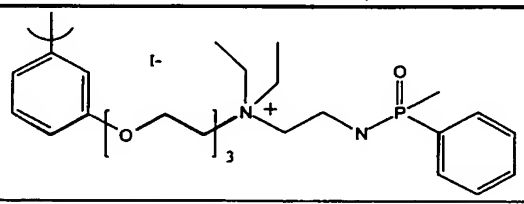
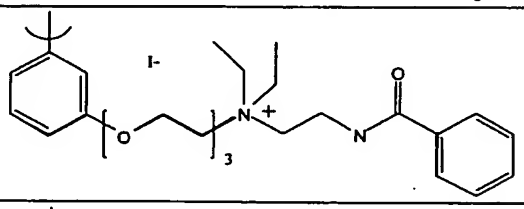
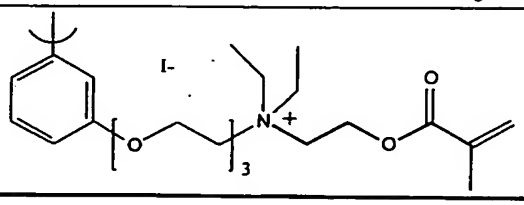
1365		n-butyl	OH	H
1366		n-butyl	OH	H
1367		n-butyl	OH	H

1368		n-butyl	OH	H
1369		n-butyl	OH	H

1370	n-butyl	n-butyl	OH	H	
1371	n-butyl	n-butyl	OH	H	
1372	n-butyl	n-butyl	OH	H	

1373	n-butyl	n-butyl	OH	H	
1374	n-butyl	n-butyl	OH	H	
1375	n-butyl	n-butyl	OH	H	

1376	n-butyl	n-butyl	OH	H	
1377	n-butyl	n-butyl	OH	H	
1378	n-butyl	n-butyl	OH	H	
1379	n-butyl	n-butyl	OH	H	

1380	n-butyl	n-butyl	OH	H	
1381	n-butyl	n-butyl	OH	H	
1382	n-butyl	n-butyl	OH	H	

	H	OH	n-butyl	n-butyl	1383
	H	OH	n-butyl	n-butyl	1384
	H	OH	n-butyl	n-butyl	1385

163

	H	OH	n-butyl	n-butyl	1386
	H	OH	n-butyl	n-butyl	1387
	H	OH	n-butyl	n-butyl	1388

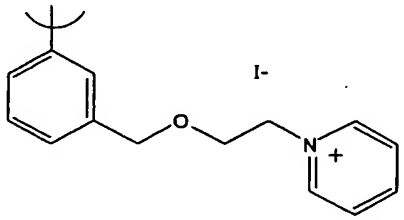
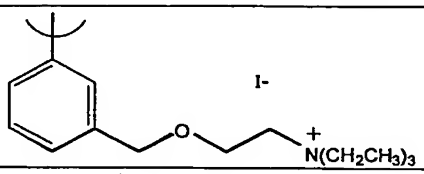
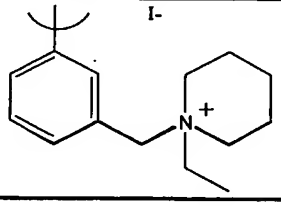
164

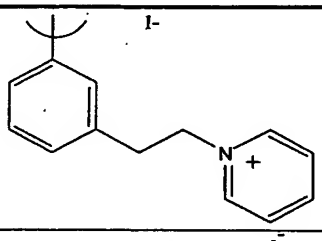
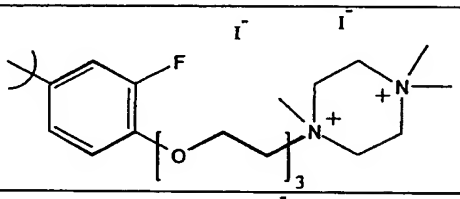
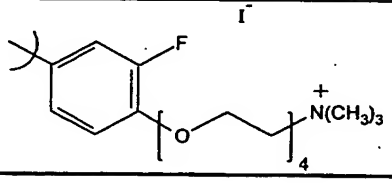
165

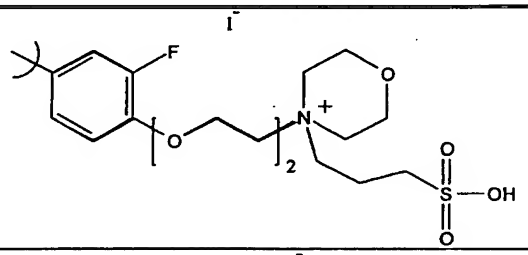
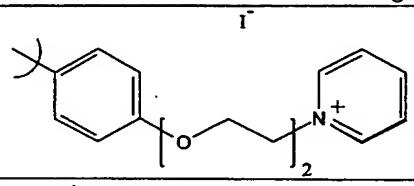
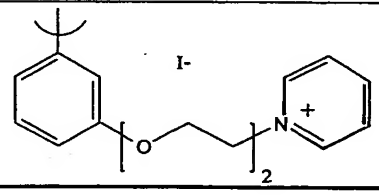
1389	n-butyl	n-butyl	OH	H
1390	n-butyl	n-butyl	OH	H
1391	n-butyl	n-butyl	OH	H

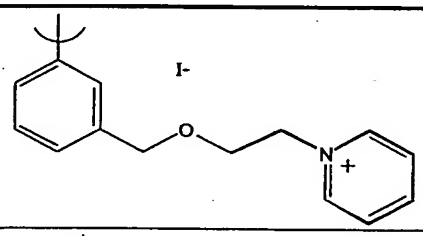
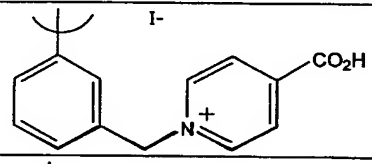
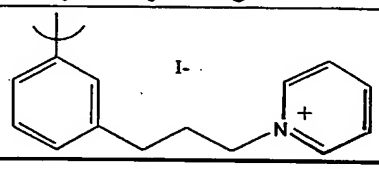
166

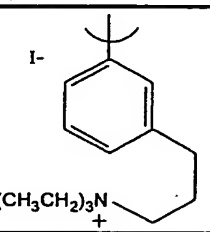
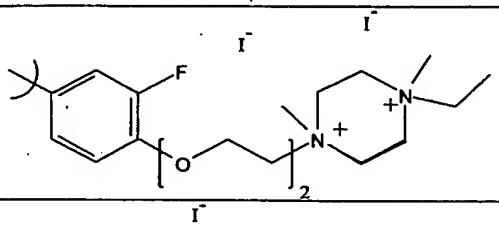
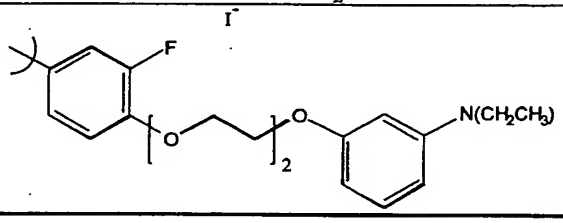
1392	n-butyl	n-butyl	OH	H
1393	n-butyl	n-butyl	OH	H
1394	n-butyl	n-butyl	OH	H

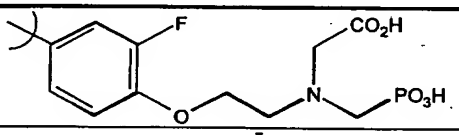
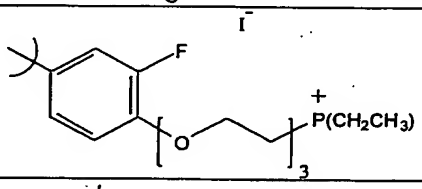
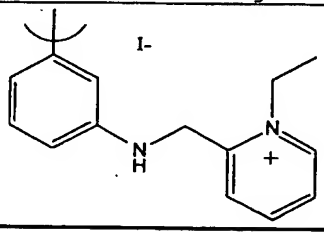
1395	n-butyl	n-butyl	OH	H	
1396	n-butyl	n-butyl	OH	H	
1397	n-butyl	n-butyl	OH	H	

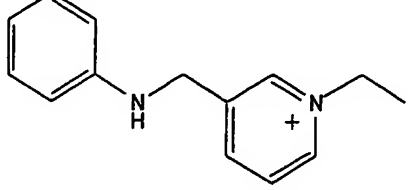
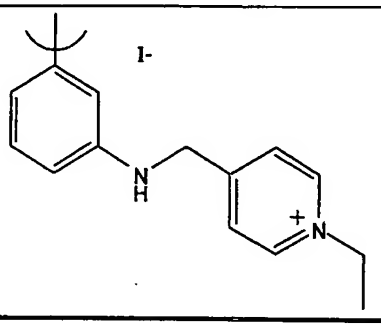
1398	n-butyl	n-butyl	OH	H	
1399	n-butyl	n-butyl	OH	H	
1400	n-butyl	n-butyl	OH	H	

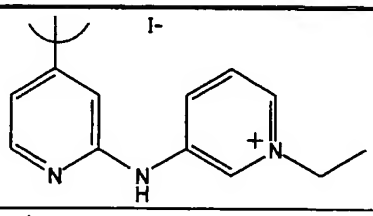
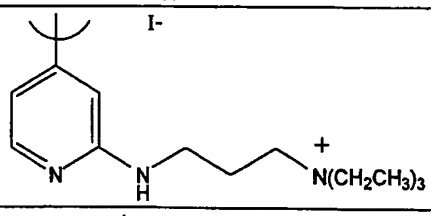
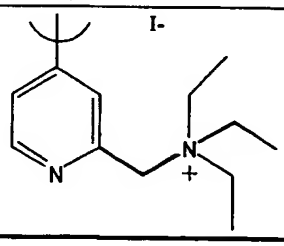
1401	n-butyl	n-butyl	OH	H	
1402	n-butyl	n-butyl	OH	H	
1403	n-butyl	n-butyl	OH	H	

1404	n-butyl	n-butyl	OH	H	
1405	n-butyl	n-butyl	OH	H	
1406	n-butyl	n-butyl	OH	H	

1407	n-butyl	n-butyl	OH	H	
1408	n-butyl	n-butyl	OH	H	
1409	n-butyl	n-butyl	OH	H	

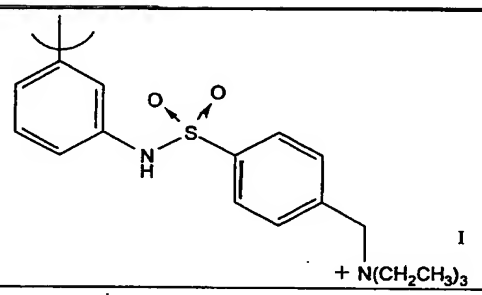
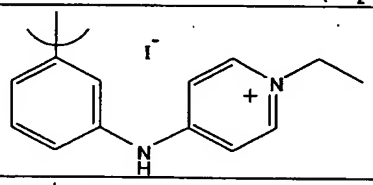
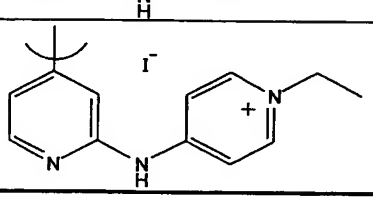
1410	n-butyl	n-butyl	OH	H	
1411	n-butyl	n-butyl	OH	H	
1412	n-butyl	n-butyl	OH	H	

					
1414	n-butyl	n-butyl	OH	H	

1415	n-butyl	n-butyl	OH	H	
1416	n-butyl	n-butyl	OH	H	
1417	n-butyl	n-butyl	OH	H	

1418	n-butyl	n-butyl	OH	H	
1419	n-butyl	n-butyl	OH	H	

1420	n-butyl	n-butyl	OH	H	
1421	n-butyl	n-butyl	OH	H	

1422	n-butyl	n-butyl	OH	H	 I
1423	n-butyl	n-butyl	OH	H	
1424	n-butyl	n-butyl	OH	H	

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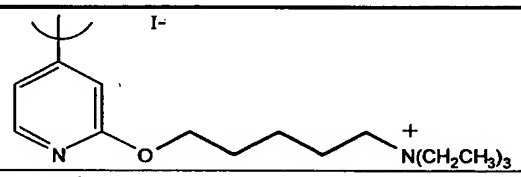
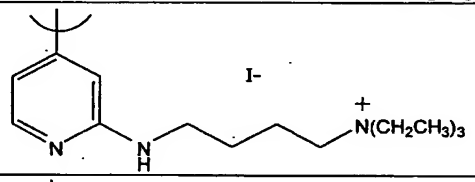
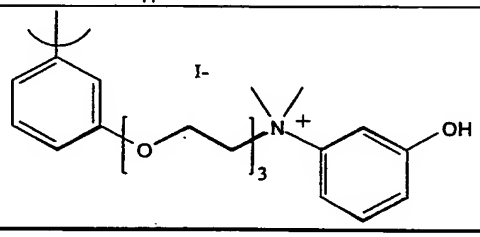
1425	n-butyl	n-butyl	OH	H	
1426	n-butyl	n-butyl	OH	H	
1427	n-butyl	n-butyl	OH	H	

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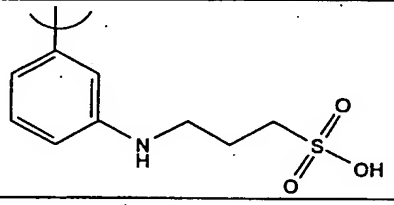
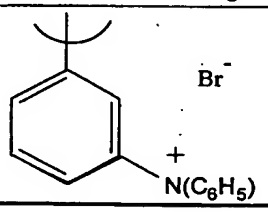
1428	n-butyl	n-butyl	OH	H	
1429	n-butyl	n-butyl	OH	H	

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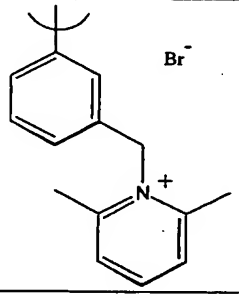
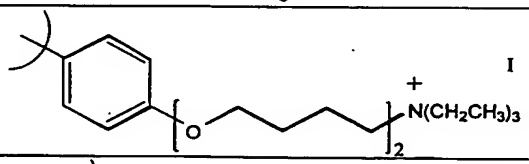
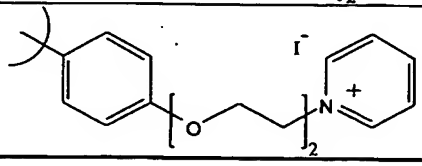
1430	n-butyl	n-butyl	OH	H	
1431	n-butyl	n-butyl	OH	H	
1432	n-butyl	n-butyl	OH	H	

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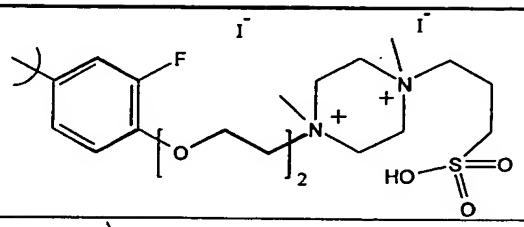
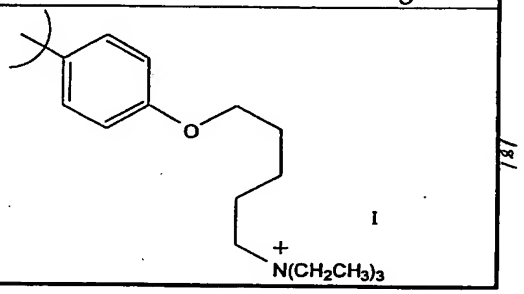
1433	n-butyl	n-butyl	OH	H	
1434	n-butyl	n-butyl	OH	H	

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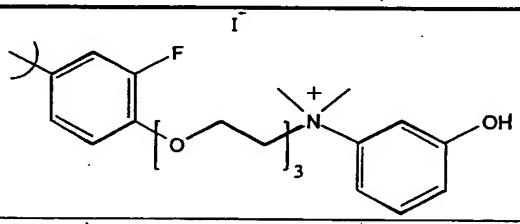
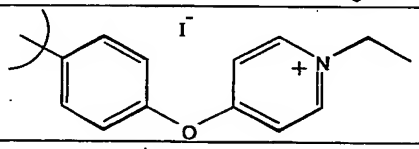
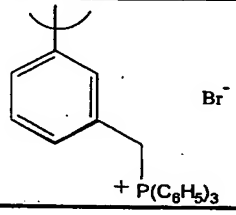
1435	n-butyl	n-butyl	OH	H	
1436	n-butyl	n-butyl	OH	H	
1437	n-butyl	n-butyl	OH	H	

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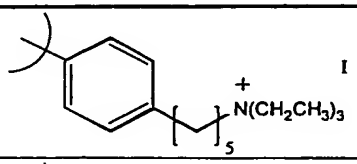
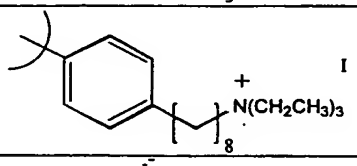
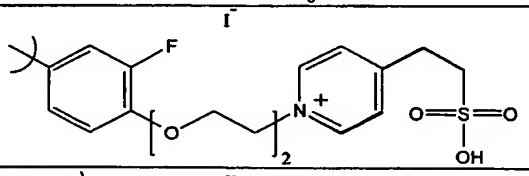
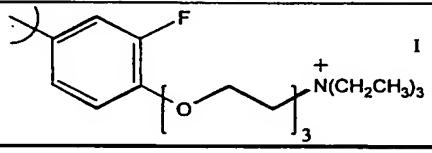
1438	n-butyl	n-butyl	OH	H	
1439	n-butyl	n-butyl	OH	H	
1440	n-butyl	n-butyl	OH	H	
1441	n-butyl	n-butyl	OH	H	

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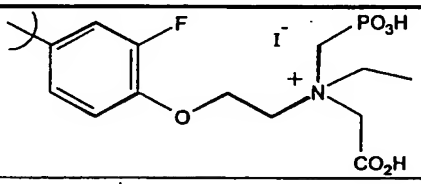
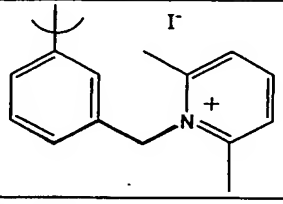
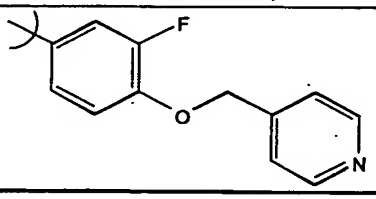
1442	n-butyl	n-butyl	OH	H	
1443	n-butyl	n-butyl	OH	H	
1444	n-butyl	n-butyl	OH	H	

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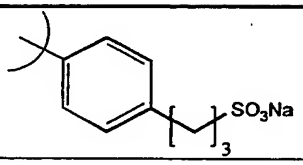
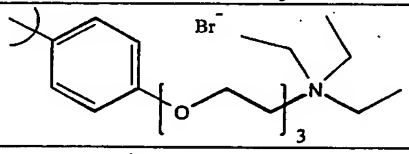
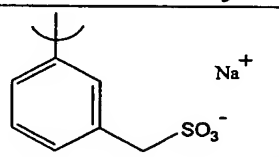
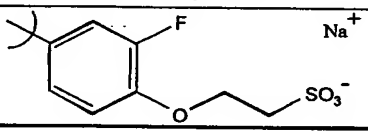
1445	n-butyl	n-butyl	OH	H	
1446	n-butyl	n-butyl	OH	H	
1447	n-butyl	n-butyl	OH	H	
1448	n-butyl	n-butyl	OH	H	

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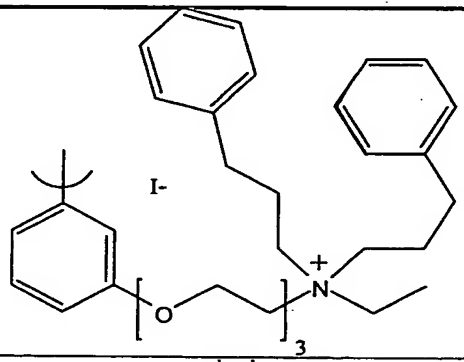
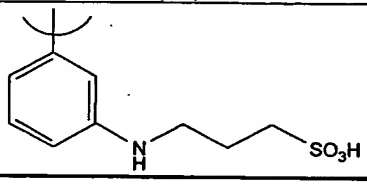
1449	n-butyl	n-butyl	OH	H	
1450	n-butyl	n-butyl	OH	H	phenyl
1451	n-butyl	n-butyl	OH	H	

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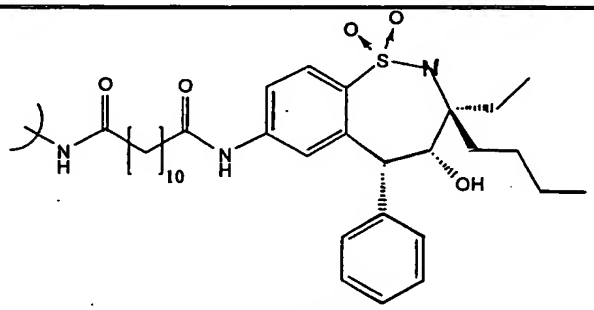
Compound Number	R^6	$(R^x)_q$
101	H	 at the 7-position
102	H	7-trimethylammonium iodide
103	H	7-trimethylammonium iodide
104	H	7-dimethylamino
105	H	7-methanesulfonamido
106	H	7-(2'-bromoacetamido)
107	H	7-amino
108	H	7-(hexylamido)
109	H	7-amino
110	H	7-acetamido
111	H	7-amino
112	H	7-amino
113	H	7-amino
114	H	7-amino

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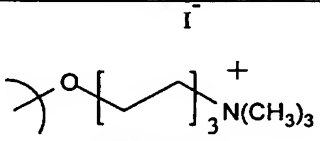
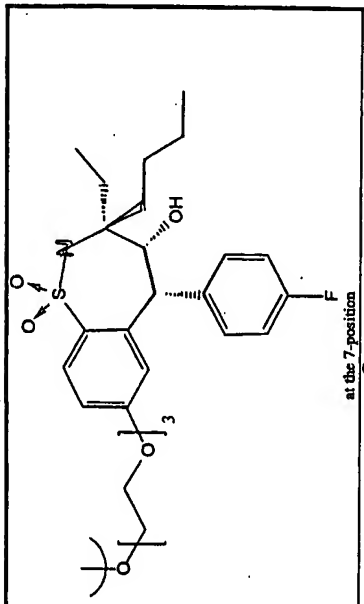
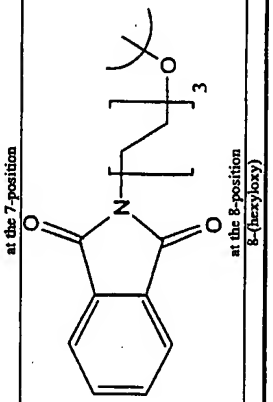
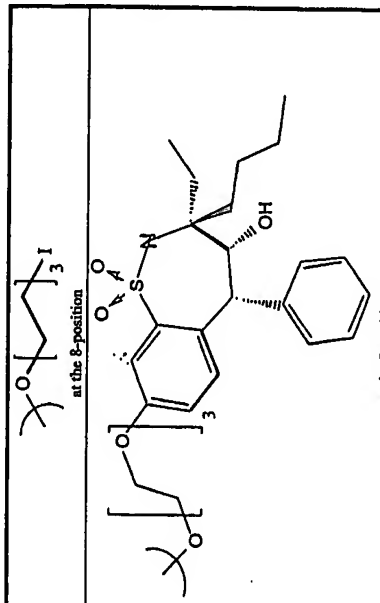
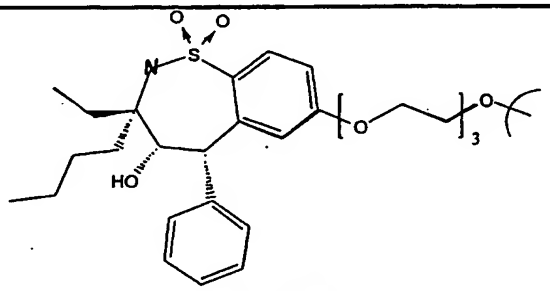
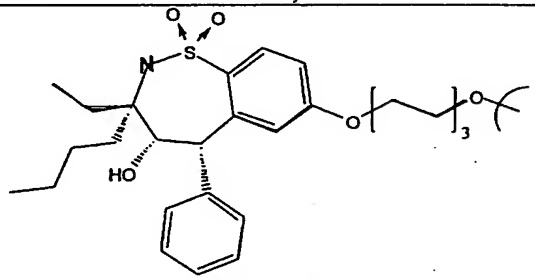
115	H	7-(O-benzylcarbamato)
116	H	7-(O-benzylcarbamato)
117	H	7-(O-benzylcarbamato)
118	H	7-(O-benzylcarbamato)
119	H	7-(O-tert-butylcarbamato)
120	H	7-(O-benzylcarbamato)
121	H	7-amino
122	H	7-amino
123	H	7-hexylamino
124	H	7-(hexylamino)
125	H	 at the 8-position
126	H	7-(O-benzylcarbamato)
127	H	7-amino
128	H	7-(O-benzylcarbamato)
129	H	7-amino

188

131	H	 at the 7-position
132	H	 at the 8-position 8-(hexyloxy)
133	H	

134	H	 at the 8-position
135	H	
136	H	at the 8-position 8-hydroxy

137	H	 at the 7-position
138	H	8-acetoxy
139	H	 at the 7-position

142	3-methoxy-phenyl	7-methylmercapto
143	H	7-methylmercapto
144	H	7-(N-azetidinyl)
262	H	7-methoxy
263	3-methoxy-phenyl	7-methoxy
264	H	7-methoxy
265	3-trifluoro-methyl-phenyl	7-methoxy
266	H	7-hydroxy
267	H	7-methoxy
268	H	7-methoxy
269	4-fluoro-phenyl	7-methoxy
270	H	7-hydroxy
271	H	7-bromo
272	3-methoxy-phenyl	7-bromo
273	4-fluoro-phenyl	7-fluoro
274	H	7-fluoro
275	3-methoxy-phenyl	7-fluoro
276	H	7-fluoro
277	H	7-methoxy
278	H	7-methoxy
279	H	7-methoxy
280	H	7-methoxy
281	H	7-methylmercapto
282	H	7-methyl
283	4-fluoro-phenyl	7-methyl
284	H	7-(4'-morpholino)
286	H	7-(O-benzylcarbamato)
287	H	7-amino
288	H	7-amino
289	H	7-amino

290	H	7-amino
291	H	7-(O-benzylcarbamato)
292	H	7-amino
293	H	7-benzylamino
294	H	7-dimethylamino
295	H	7-amino
296	H	7-amino
1000	H	7-dimethylamino
1001	H	7-dimethylamino
1002	H	7-dimethylamino
1003	H	7-dimethylamino
1004	H	7-dimethylamino
1005	H	7-dimethylamino
1006	H	7-dimethylamino
1007	H	7-dimethylamino
1008	H	7-dimethylamino
1009	H	7-dimethylamino
1010	H	7-dimethylamino
1011	H	7-dimethylamino
1012	H	7-dimethylamino; 9-methoxy
1013	H	7-dimethylamino
1014	H	7-dimethylamino; 9-methoxy
1015	H	7-dimethylamino
1016	H	7-dimethylamino
1017	H	7-dimethylamino
1018	H	7-dimethylamino
1019	H	7-dimethylamino
1020	H	7-dimethylamino
1021	H	7-dimethylamino
1022	H	7-dimethylamino
1023	H	7-dimethylamino
1024	H	7-dimethylamino
1025	H	7-dimethylamino

1026	H	7-dimethylamino
1027	H	7-dimethylamino
1028	H	7-dimethylamino
1029	H	7-dimethylamino
1030	H	7-dimethylamino
1031	H	7-dimethylamino
1032	H	7-dimethylamino
1033	H	7-dimethylamino
1034	H	7-dimethylamino
1035	H	7-dimethylamino
1036	H	7-dimethylamino
1037	H	7-dimethylamino
1038	H	7-dimethylamino
1039	H	7-dimethylamino
1040	H	7-dimethylamino
1041	H	7-dimethylamino
1042	H	7-dimethylamino
1043	H	7-dimethylamino
1044	H	7-dimethylamino
1045	H	7-dimethylamino
1046	H	7-dimethylamino
1047	H	7-dimethylamino
1048	H	7-dimethylamino
1049	H	7-dimethylamino
1050	H	7-dimethylamino
1051	H	7-dimethylamino
1052	H	7-dimethylamino
1053	H	7-dimethylamino
1054	H	7-dimethylamino
1055	H	7-dimethylamino
1056	H	7-dimethylamino
1057	H	7-dimethylamino
1058	H	7-dimethylamino

1059	H	7-dimethylamino
1060	H	7-methylamino
1061	H	7-methylamino
1062	H	7-methylamino
1063	H	7-methylamino
1064	H	7-methylamino
1065	H	7-dimethylamino
1066	H	7-dimethylamino
1067	H	9-dimethylamino
1068	H	7-dimethylamino
1069	H	7-dimethylamino; 9-dimethylamino
1070	H	7-dimethylamino
1071	H	7-dimethylamino
1072	H	7-dimethylamino
1073	H	7-dimethylamino
1074	H	7-dimethylamino
1075	H	7-dimethylamino; 9-dimethylamino
1076	H	7-dimethylamino
1077	H	7-dimethylamino
1078	H	7-dimethylamino
1079	H	7-dimethylamino
1080	H	7-dimethylamino
1081	H	7-dimethylamino
1082	H	7-dimethylamino
1083	H	7-dimethylamino
1084	H	7-dimethylamino
1085	H	7-dimethylamino
1086	H	7-dimethylamino
1087	H	7-dimethylamino
1088	H	7-dimethylamino
1089	H	7-dimethylamino
1090	H	7-dimethylamino

1091	H	7-dimethylamino
1092	H	7-dimethylamino
1093	H	7-dimethylamino
1094	H	7-dimethylamino
1095	H	7-dimethylamino
1096	H	7-dimethylamino
1097	H	7-dimethylamino
1098	H	7-dimethylamino
1099	H	7-dimethylamino
1100	H	7-dimethylamino
1101	H	7-dimethylamino
1102	H	7-dimethylamino
1103	H	7-dimethylamino
1104	H	7-dimethylamino
1105	H	7-dimethylamino
1106	H	7-dimethylamino
1107	H	7-dimethylamino
1108	H	7-dimethylamino
1109	H	7-dimethylamino
1110	H	7-dimethylamino
1111	H	7-dimethylamino
1112	H	7-dimethylamino
1113	H	7-dimethylamino
1114	H	7-methylamino
1115	H	7-dimethylamino
1116	H	7-dimethylamino
1117	H	7-dimethylamino
1118	H	7-dimethylamino
1119	H	7-dimethylamino
1120	H	7-dimethylamino
1121	H	7-dimethylamino
1122	H	7-dimethylamino
1123	H	7-dimethylamino

1124	H	7-dimethylamino
1125	H	7-dimethylamino
1126	H	7-dimethylamino
1127	H	7-dimethylamino
1128	H	7-dimethylamino
1129	H	9-dimethylamino
1130	H	7-dimethylamino
1131	H	7-dimethylamino
1132	H	7-dimethylamino
1133	H	7-dimethylamino
1134	H	7-dimethylamino
1135	H	7-dimethylamino
1136	H	7-dimethylamino
1137	H	9-(2',2'-dimethylhydrazino)
1138	H	7-dimethylamino
1139	H	7-dimethylamino
1140	H	7-(2',2'-dimethylhydrazino)
1141	H	7-ethylmethylamino
1142	H	7-dimethylamino
1143	3-fluoro-4-methoxy-phenyl	7-dimethylamino
1144	H	7-dimethylamino
1145	H	9-dimethylamino
1146	H	7-dimethylamino
1147	H	7-diethylamino
1148	H	7-dimethylsulfonium, fluoride salt
1149	H	7-ethylamino
1150	H	7-ethylmethylamino
1151	H	7-dimethylamino
1152	H	7-(ethoxymethyl) methylamino
1153	H	7-methylamino
1154	H	9-methoxy
1155	H	7-methyl

1156	H	7-methylmercapto
1157	H	7-fluoro; 9-dimethylamino
1158	H	7-methoxy
1159	H	7-dimethylamino
1160	H	7-diethylamino
1161	H	7-dimethylamino
1162	H	7-dimethylamino
1163	H	7-methoxy
1164	H	7-methoxy
1165	H	7-trimethylammonium iodide
1166	H	7-trimethylammonium iodide
1167	H	7-dimethylamino
1168	H	7-trimethylammonium iodide
1169	H	8-dimethylamino
1170	H	7-ethylpropylamino
1171	H	7-dimethylamino
1172	H	7-methoxy
1173	H	7-ethylpropylamino
1174	H	7-phenyl
1175	H	7-methylsulfonyl
1176	H	9-fluoro
1177	H	7-butylmethylamino
1178	H	7-dimethylamino
1179	H	8-methoxy
1180	H	7-trimethylammonium iodide
1181	H	7-butylmethylamino
1182	H	7-methoxy
1183	H	7-fluoro
1184	H	7-fluoro; 9-fluoro
1185	H	7-fluoro
1186	H	7-fluoro; 9-fluoro
1187	H	7-methyl

1188	H	7-trimethylammonium iodide
1189	H	7-trimethylammonium iodide
1190	H	7-bromo
1191	H	7-hydroxy
1192	H	7-hydroxy
1193	H	7-dimethylamino
1194	H	7-dimethylamino
1195	H	7-(4'-methylpiperazin-1-yl)
1196	H	7-methoxy
1197	H	7-(N-methylformamido)
1198	H	7-methoxy
1199	H	7-dimethylamino
1200	phenyl	7-dimethylamino
1201	H	7-methyl
1202	H	7-methoxy
1203	H	7-(4'-tert-butylphenyl)
1204	H	7-methoxy
1205	H	7-dimethylamino
1206	H	7-dimethylamino
1207	H	7-dimethylamino
1208	H	7-dimethylamino
1209	H	7-dimethylphenyl
1210	H	7-dimethylamino
1211	H	7-dimethylamino
1212	H	9-(4'-morpholino)
1213	3-fluoro-4-methoxy-phenyl	7-dimethylamino
1214	H	7-(N-methylformamido)
1215	H	9-methylmercapto
1216	H	7-bromo
1217	H	7-dimethylamino
1218	H	9-methylsulfonyl
1219	H	7-dimethylamino

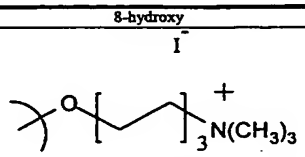
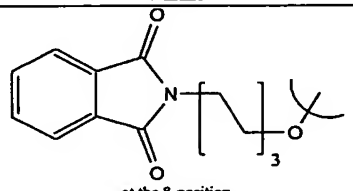
1220	H	7-isopropylamino
1221	H	7-dimethylamino
1222	H	7-ethylamino
1223	H	8-bromo; 7-methylamino
1224	H	7-fluoro
1225	H	7-dimethylamino
1226	H	7-bromo
1227	H	7-(tert-butylamino
1228	H	8-bromo; 7-dimethylamino
1229	H	7-dimethylamino
1230	H	9-dimethylamino; 7-fluoro
1231	H	7-dimethylamino
1232	H	9-dimethylamino
1233	H	7-dimethylamino
1234	H	7-dimethylamino
1235	H	7-dimethylamino
1236	H	7-dimethylamino
1237	H	7-dimethylamino
1238	H	7-dimethylamino
1239	H	7-dimethylamino
1240	H	7-dimethylamino
1241	H	7-dimethylamino
1242	H	7-dimethylamino
1243	H	7-dimethylamino
1244	H	7-(1'-methylhydrazido)
1245	H	7-dimethylamino
1246	H	7-dimethylamino
1247	H	7-dimethylamino
1248	H	7-dimethylamino
1249	H	7-dimethylamino

1250	H	7-dimethylamino
1251	H	7-dimethylamino
1252	H	7-dimethylamino
1253	H	7-dimethylamino
1254	H	7-dimethylamino
1255	H	7-dimethylamino
1256	H	7-dimethylamino
1257	H	8-bromo; 7-dimethylamino
1258	H	9-(tert-butylamino)
1259	phenyl	7-dimethylamino
1260	H	7-dimethylamino
1261	H	7-dimethylamino
1262	H	7-dimethylamino
1263	H	7-bromo
1264	H	7-isopropylamino
1265	H	9-isopropylamino
1266	H	7-dimethylamino
1267	H	7-carboxy, methyl ester
1268	H	7-dimethylamino
1269	H	7-dimethylamino
1270	H	7-dimethylamino
1271	H	7-dimethylamino
1272	H	7-dimethylamino
1273	H	7-dimethylamino
1274	H	7-dimethylamino
1275	H	7-dimethylamino
1276	H	7-dimethylamino
1277	H	7-dimethylamino
1278	H	7-dimethylamino
1279	H	7-dimethylamino
1280	H	7-dimethylamino
1281	H	7-dimethylamino
1282	H	7-trimethylammonium iodide

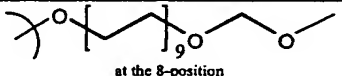
201

1283	H	7-dimethylamino
1284	H	9-ethylamino
1285	H	7-dimethylamino
1286	H	7-dimethylamino
1287	H	7-dimethylamino
1288	H	7-dimethylamino
1289	H	7-dimethylamino
1290	H	7-dimethylamino
1291	H	7-dimethylamino
1292	H	7-dimethylammio
1293	H	7-dimethylamino
1294	H	7-dimethylamino
1295	H	7-dimethylamino
1296	H	7-dimethylamino
1297	H	7-dimethylamino
1298	H	7-dimethylamino
1299	H	7-dimethylamino
1300	phenyl	7-dimethylamino
1301	H	7-trimethylammonium iodide
1302	H	9-hydroxy
1303	H	7-dimethylamino
1304	H	7-tert-butylamino
1305	H	9-methylamino
1306	H	7-dimethylamino
1307	4-methoxy-phenyl	9-(4'-morpholino)
1308	H	7-dimethylamino
1309	H	9-fluoro
1310	H	7-amino
1311	H	7-(hydroxylamino)
1312	H	8-hexyloxy
1313	H	8-ethoxy
1314	H	7-(hydroxylamino)
1315	H	7-(hexyloxy)

202

1316	H	8-hydroxy
1317	H	 at the 8-position
1318	H	7-dimethylamino
1319	H	7-fluoro
1320	H	7-amino
1321	H	 at the 8-position
1322	H	7-dimethylamino
1323	H	7-dimethylamino
1324	H	7-dimethylamino
1325	H	7-dimethylamino
1326	H	7-dimethylamino
1327	H	7-dimethylamino
1328	H	7-dimethylamino
1329	H	7-dimethylamino
1330	H	7-dimethylamino
1331	H	7-dimethylamino
1332	H	7-dimethylamino

203

1333	H	7-dimethylamino
1334	H	7-dimethylamino
1335	H	7-dimethylamino
1336	H	7-dimethylamino
1337	H	7-dimethylamino
1338	H	7-(4'-methylpiperazinyl)
1339	H	7-dimethylamino
1340	H	7-methyl
1341	H	7-dimethylamino
1342	H	7-(4'-fluorophenyl)
1343	H	7-amino
1344	H	7-dimethylamino
1345	H	7-trimethylammonium iodide
1346	H	 at the 8-position
1347	H	7-dimethylamino
1348	H	7-dimethylamino
1349	H	7-dimethylamino
1350	H	7-trimethylammonium iodide
1351	H	7-dimethylamino
1352	H	7-dimethylamino
1353	H	7-dimethylamino
1354	H	7-dimethylamino
1355	H	7-dimethylamino
1356	H	7-dimethylamino
1357	H	7-dimethylamino
1358	H	7-dimethylamino
1359	H	7-dimethylamino
1360	H	7-dimethylamino
1361	H	7-dimethylamino
1362	H	7-dimethylamino

204

1363	H	7-dimethylamino
1364	H	7-dimethylamino
1365	H	7-dimethylamino
1366	H	7-dimethylamino
1367	H	7-dimethylamino
1368	H	7-dimethylamino
1369	H	7-dimethylamino
1370	H	7-dimethylamino
1371	H	7-dimethylamino
1372	H	7-dimethylamino
1373	H	7-dimethylamino
1374	H	7-dimethylamino
1375	H	7-dimethylamino
1376	H	7-dimethylamino
1377	H	7-dimethylamino
1378	H	7-dimethylamino
1379	H	7-dimethylamino
1380	H	7-dimethylamino
1381	H	7-dimethylamino
1382	H	7-dimethylamino
1383	H	7-dimethylamino
1384	H	7-dimethylamino
1385	H	7-dimethylamino
1386	H	7-dimethylamino
1387	H	7-dimethylamino
1388	H	7-dimethylamino
1389	H	7-dimethylamino
1390	H	7-dimethylamino
1391	H	7-dimethylamino
1392	H	7-dimethylamino
1393	H	7-dimethylamino
1394	H	7-dimethylamino
1395	H	7-dimethylamino

1396	H	7-dimethylamino
1397	H	7-dimethylamino
1398	H	7-dimethylamino
1399	H	7-dimethylamino
1400	H	7-dimethylamino
1401	H	7-dimethylamino
1402	H	7-dimethylamino
1403	H	7-dimethylamino
1404	H	7-dimethylamino
1405	H	7-dimethylamino
1406	H	7-dimethylamino
1407	H	7-dimethylamino
1408	H	7-dimethylamino
1409	H	7-dimethylamino
1410	H	7-dimethylamino
1411	H	7-dimethylamino
1412	H	7-dimethylamino
1413	H	7-dimethylamino
1414	H	7-dimethylamino
1415	H	7-dimethylamino
1416	H	7-dimethylamino
1417	H	7-dimethylamino
1418	H	7-dimethylamino
1419	H	7-dimethylamino
1420	H	7-dimethylamino
1421	H	7-dimethylamino
1422	H	7-dimethylamino
1423	H	7-dimethylamino
1424	H	7-dimethylamino
1425	H	7-dimethylamino
1426	H	7-dimethylamino
1427	H	7-dimethylamino
1428	H	7-dimethylamino

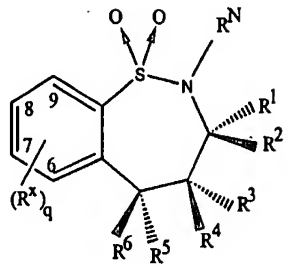
207

1429	H	7-dimethylamino
1430	H	7-dimethylamino
1431	H	7-dimethylamino
1432	H	7-dimethylamino
1433	H	7-dimethylamino
1434	H	7-dimethylamino
1435	H	7-dimethylamino
1436	H	7-dimethylamino
1437	H	7-dimethylamino
1438	H	7-dimethylamino
1439	H	7-dimethylamino
1440	H	7-dimethylamino
1441	H	7-dimethylamino
1442	H	7-dimethylamino
1443	H	7-dimethylamino
1444	H	7-dimethylamino
1445	H	7-dimethylamino
1446	H	7-methoxy; 8-methoxy
1447	H	7-dimethylamino
1448	H	7-dimethylamino
1449	H	7-dimethylamino
1450	H	7-dimethylamino
1451	H	7-dimethylamino

208

Another class of compounds of particular interest comprises those 1,2-benzothiazepines wherein the R^1, R^2, R^3, R^4, R^5, R^6, R^N and R^x radicals are selected from among the radicals disclosed in Table 2 below. Preferably, R^6 is hydrogen and R^3 is other than hydrogen; and/or R^3 is hydroxy and R^4 is hydrogen; and/or R^1 and R^2 are alkyl. More preferably, R^1 and R^2 are the same.

Table 2



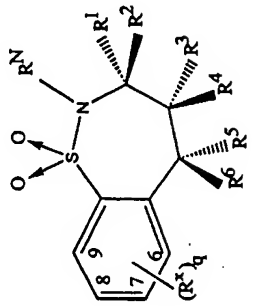
R^1/R^2	R^3/R^4	R^5/R^6	$(R^x)q$	R^N
ethyl n-propyl n-butyl n-pentyl n-hexyl iso-propyl iso-butyl iso-pentyl $CH_2OC_2H_5$ CH_2O-(4-picoline) $CH_2CH_2CH_3$ CF_3	HO- H-	H Ph- p-F-Ph- m-F-Ph- p-CH_3O-Ph- p-HO-Ph- m-CH_3O-Ph- m-HO-Ph- p-$(CH_3)_2N$-Ph- m-$(CH_3)_2N$-Ph- p-H_2N-Ph- m-H_2N-Ph- I^-, p-$(CH_3)_3$-N^+-Ph- I^-, m-$(CH_3)_3$-N^+-Ph- I^-, p-$(CH_3)_3$-N^+-CH_2CH_2-$(OCH_2CH_2)_2$-O-Ph- I^-, m-$(CH_3)_3$-N^+-CH_2CH_2-$(OCH_2CH_2)_2$-O-Ph- I^-, p-(N,N-dimethyl-piperazine)-(N')-CH_2-$(OCH_2CH_2)_2$-O-Ph- I^-, m-(N,N-dimethyl-piperazine)-(N')-CH_2-$(OCH_2CH_2)_2$-O-Ph- m-F, p-CH_3O-Ph- 3,4,dioxymethylene-Ph m-CH_3O-, p-F-Ph- 4-pyridine N-methyl-4-pyridinium, I^- 3-pyridine N-methyl-3-pyridinium, I^- 2-pyridine p-CH_3O_2C-Ph- thienyl-2-yl 5-Cl-thienyl-2-yl	7-methyl 7-ethyl 7-iso-propyl 7-tert-butyl 7-OH 7-OCH_3 7-O(iso-propyl) 7-SCH_3 7-$SOCH_3$ 7-SO_2CH_3 7-SCH_2CH_3 7-NH_2 7-NHOH 7-$NHCH_3$ 7-$N(CH_3)_2$ 7-$N^+(CH_3)_3$, I^- 7-$NHC(O)CH_3$ 7-$N(CH_2CH_3)_2$ 7-$NMeCH_2CO_2H$ 7-$N^+(Me)_2CH_2CO_2H$, I^- 7-(N)-morpholine 7-(N)-azetidine 7-(N)-N-methylazetidinium, I^- 7-(N)-pyrrolidine 7-(N)-N-methyl-pyrrolidinium, I^- 7-(N)-N-methyl-morpholinium, I^- 7-(N)-N'-methylpiperazine 7-(N)-N'-dimethylpiperazinium, I^- 7-NH-CBZ 7-$NHC(O)C_5H_{11}$ 7-$NHC(O)CH_2Br$ 7-NH-$C(NH)NH_2$ 7-(2)-thiophene 8-methyl 8-ethyl 8-iso-propyl 8-tert-butyl 8-OH 8-OCH_3	H- methyl ethyl n-propyl n-butyl n-pentyl n-hexyl benzyl

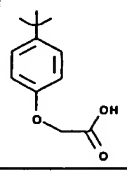
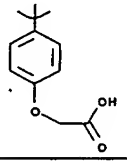
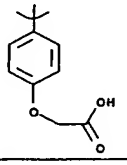
R^1/R^2	R^3/R^4	R^5/R^6	$(R^x)q$	R^N
			8-O(iso-propyl) 8-SCH_3 8-$SOCH_3$ 8-SO_2CH_3 8-SCH_2CH_3 8-NH_2 8-NHOH 8-$NHCH_3$ 8-$N(CH_3)_2$ 8-$N^+(CH_3)_3$, I^- 8-$NHC(O)CH_3$ 8-$N(CH_2CH_3)_2$ 8-$NMeCH_2CO_2H$ 8-$N^+(Me)_2CH_2CO_2H$, I^- 8-(N)-morpholine 8-(N)-azetidine 8-(N)-N-methylazetidinium, I^- 8-(N)-pyrrolidine 8-(N)-N-methyl-pyrrolidinium, I^- 8-(N)-N-methyl-morpholinium, I^- 8-(N)-N'-methylpiperazine 8-(N)-N'-dimethylpiperazinium, I^- 8-NH-CBZ 8-$NHC(O)C_5H_{11}$ 8-$NHC(O)CH_2Br$ 8-NH-$C(NH)NH_2$ 8-(2)-thiophene 9-methyl 9-ethyl 9-iso-propyl 9-tert-butyl 9-OH 9-OCH_3 9-O(iso-propyl) 9-SCH_3 9-$SOCH_3$ 9-SO_2CH_3 9-$N^+(Me)_2CH_2CO_2H$, I^-	

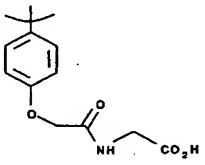
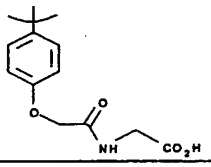
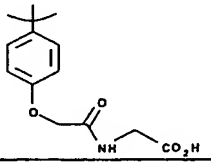
R^1/R^2	R^3/R^4	R^5/R^6	$(R^X)q$	R^N
			9-SCH_2CH_3 9-NH_2 9-NHOH 9-$NHCH_3$ 9-$N(CH_3)_2$ 9-$N^+(CH_3)_3$, I^- 9-$NHC(O)CH_3$ 9-$N(CH_2CH_3)_2$ 9-$NMeCH_2CO_2H$ 9-(N)-morpholine 9-(N)-azetidine 9-(N)-N-methylazetidinium, I^- 9-(N)-pyrrolidine 9-(N)-N-methyl-pyrrolidinium, I^- 9-(N)-N-methyl-morpholinium, I^- 9-(N)-N'-methylpiperazine 9-(N)-N'-dimethyl-piperazinium, I^- 9-NH-CBZ 9-$NHC(O)C_5H_{11}$ 9-$NHC(O)CH_2Br$ 9-$NH\text{-}C(NH)NH_2$ 9-(2)-thiophene 7-OCH_3, 8-OCH_3 7-SCH_3, 8-OCH_3 7-SCH_3, 8-SCH_3 6-OCH_3, 7-OCH_3, 8-OCH_3	

Another class of compounds of particular interest comprises those 1,2-benzothiazepines wherein the R^1, R^2, R^3, R^4 and R^5 radicals are as set forth in Table 3 below; R^6 is hydrogen; the R^N radical is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl and benzyl; and the R^x radical or radicals are independently selected from the group of R^x radicals disclosed in Table 2 above. In one embodiment of the compounds of Table 3, for example, q is 1 and R^X is 7-dimethylamino.

Table 3



Compound Number	R^1	R^2	R^3	R^4	R^5
1452	ethyl	n-butyl	OH	H	
1453	n-butyl	ethyl	OH	H	
1454	n-butyl	n-butyl	OH	H	

1455	ethyl	n-butyl	OH	H	
1456	n-butyl	ethyl	OH	H	
1457	n-butyl	n-butyl	OH	H	

215

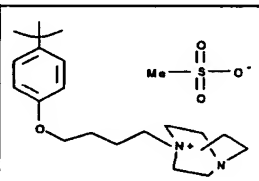
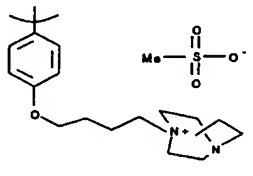
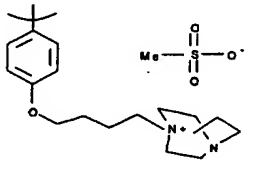
1458	ethyl	n-butyl	OH	H	
1459	n-butyl	ethyl	OH	H	
1460	n-butyl	n-butyl	OH	H	

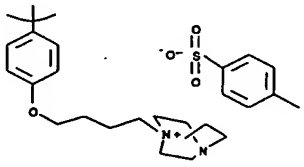
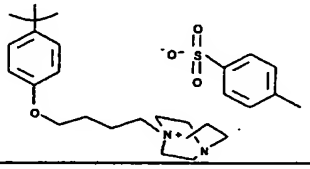
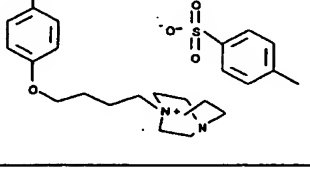
216

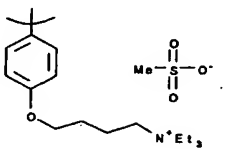
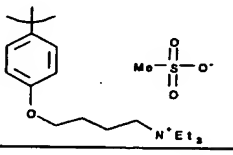
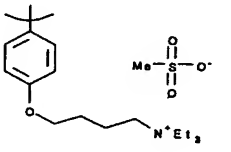
1461	ethyl	n-butyl	OH	H	
1462	n-butyl	ethyl	OH	H	
1463	n-butyl	n-butyl	OH	H	

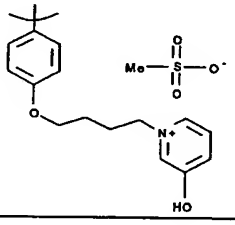
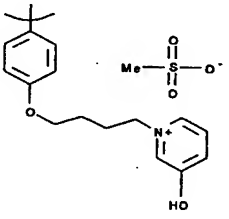
1464	ethyl	n-butyl	OH	H
1465	n-butyl	ethyl	OH	H
1466	n-butyl	n-butyl	OH	H

1467	ethyl	n-butyl	OH	H
1468	n-butyl	ethyl	OH	H
1469	n-butyl	n-butyl	OH	H

1470	ethyl	n-butyl	OH	H	
1471	n-butyl	ethyl	OH	H	
1472	n-butyl	n-butyl	OH	H	

1473	ethyl	n-butyl	OH	H	
1474	n-butyl	ethyl	OH	H	
1475	n-butyl	n-butyl	OH	H	

1476	ethyl	n-butyl	OH	H	
1477	n-butyl	ethyl	OH	H	
1478	n-butyl	n-butyl	OH	H	

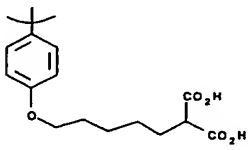
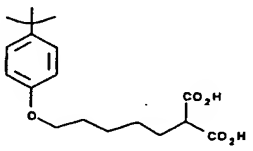
1479	ethyl	n-butyl	OH	H	
1480	n-butyl	ethyl	OH	H	

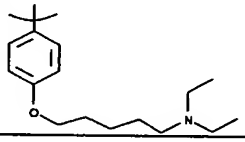
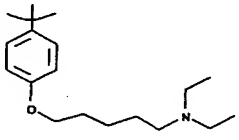
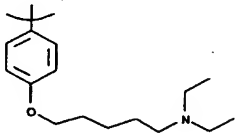
223

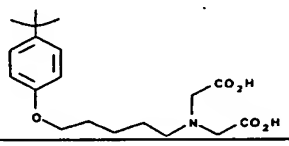
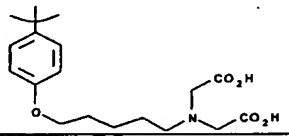
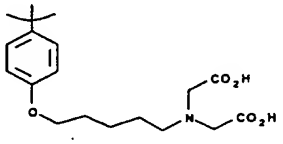
1481	n-butyl	n-butyl	OH	H
1482	ethyl	n-butyl	OH	H

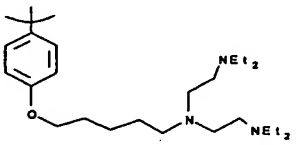
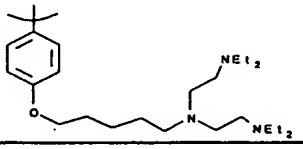
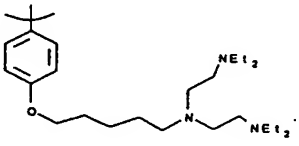
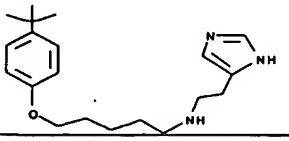
224

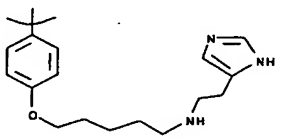
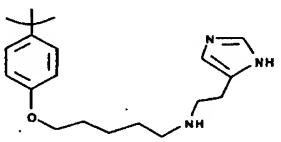
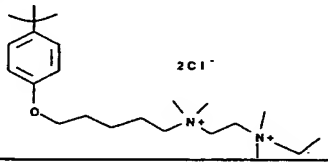
1483	n-butyl	ethyl	OH	H
1484	n-butyl	n-butyl	OH	H
1485	ethyl	n-butyl	OH	H

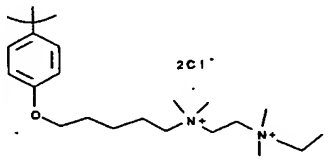
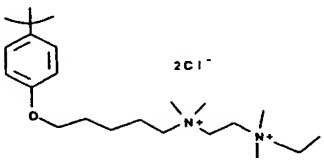
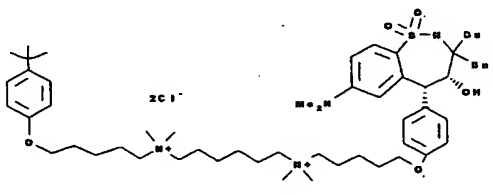
1486	n-butyl	ethyl	OH	H	
1487	n-butyl	n-butyl	OH	H	

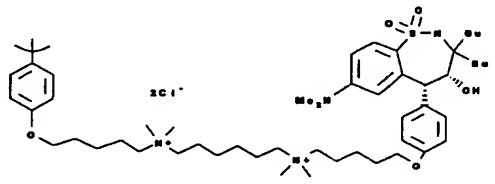
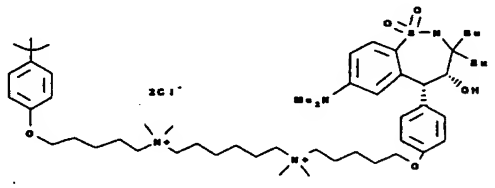
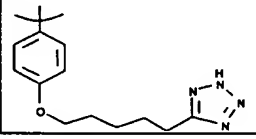
1488	ethyl	n-butyl	OH	H	
1489	n-butyl	ethyl	OH	H	
1490	n-butyl	n-butyl	OH	H	

1491	ethyl	n-butyl	OH	H	
1492	n-butyl	ethyl	OH	H	
1493	n-butyl	n-butyl	OH	H	

1494	ethyl	n-butyl	OH	H	
1495	n-butyl	ethyl	OH	H	
1496	n-butyl	n-butyl	OH	H	
1497	ethyl	n-butyl	OH	H	

1498	n-butyl	ethyl	OH	H	
1499	n-butyl	n-butyl	OH	H	
1500	ethyl	n-butyl	OH	H	

1501	n-butyl	ethyl	OH	H	
1502	n-butyl	n-butyl	OH	H	
1503	ethyl	n-butyl	OH	H	

1504	n-butyl	ethyl	OH	H	
1505	n-butyl	n-butyl	OH	H	
1506	ethyl	n-butyl	OH	H	

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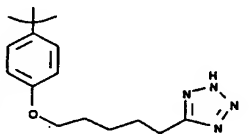
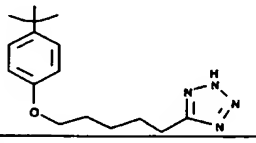
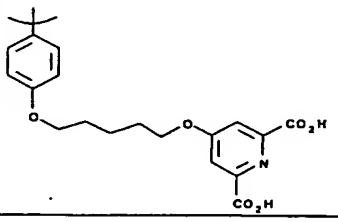
1507	n-butyl	ethyl	OH	H	
1508	n-butyl	n-butyl	OH	H	
1509	ethyl	n-butyl	OH	H	

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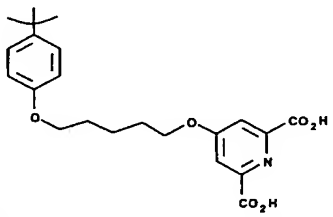
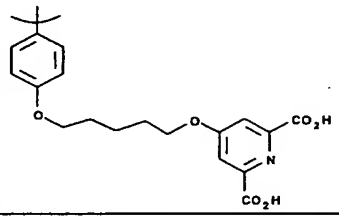
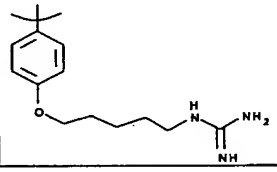
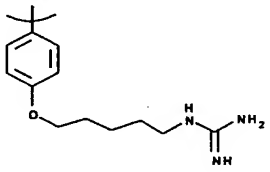
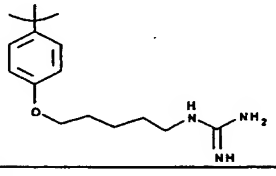
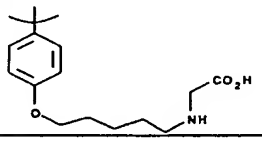
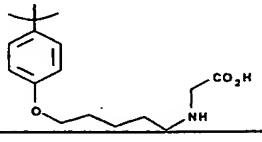
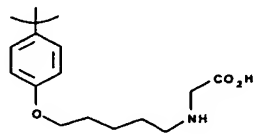
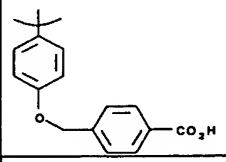
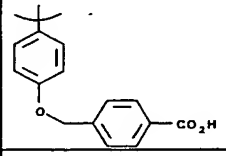
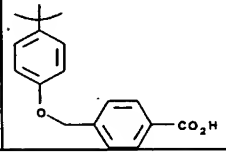
1510	n-butyl	ethyl	OH	H	
1511	n-butyl	n-butyl	OH	H	
1512	ethyl	n-butyl	OH	H	

1513	n-butyl	ethyl	OH	H	
1514	n-butyl	n-butyl	OH	H	
1515	ethyl	n-butyl	OH	H	
1516	n-butyl	ethyl	OH	H	

1517	n-butyl	n-butyl	OH	H	
1518	ethyl	n-butyl	OH	H	
1519	n-butyl	ethyl	OH	H	
1520	n-butyl	n-butyl	OH	H	

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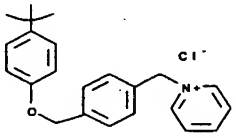
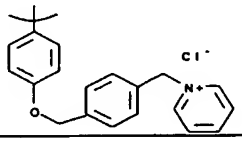
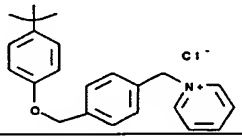
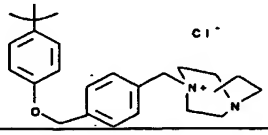
1521	ethyl	n-butyl	OH	H	
1522	n-butyl	n-butyl	OH	H	
1523	n-butyl	n-butyl	OH	H	
1524	ethyl	n-butyl	OH	H	

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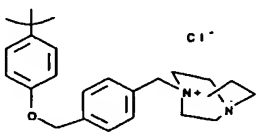
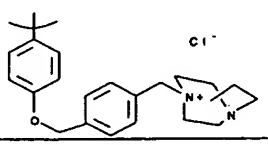
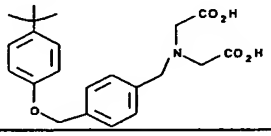
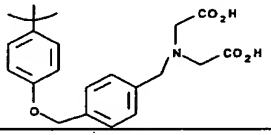
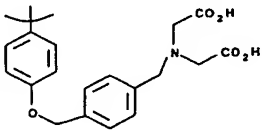
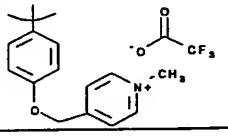
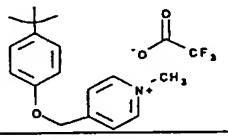
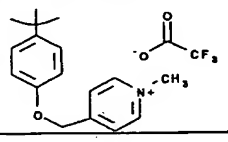
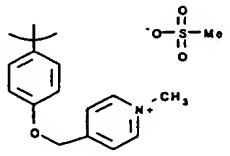
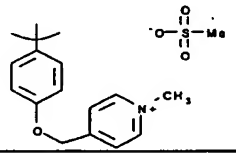
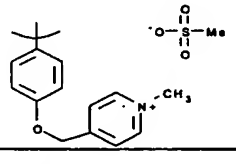
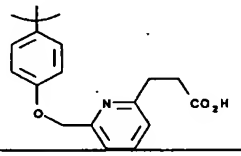
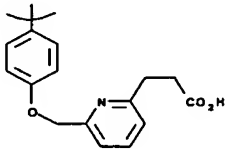
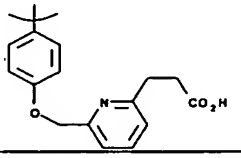
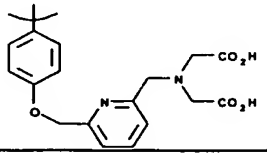
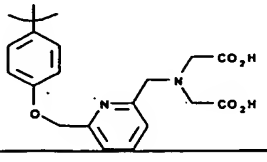
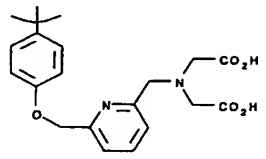
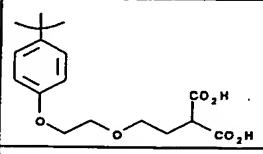
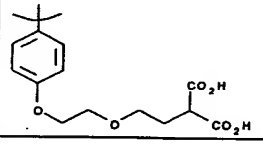
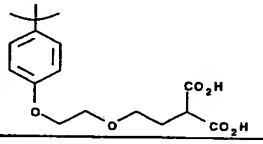
1525	n-butyl	ethyl	OH	H	
1526	n-butyl	n-butyl	OH	H	
1527	ethyl	n-butyl	OH	H	
1528	n-butyl	ethyl	OH	H	

1529	n-butyl	n-butyl	OH	H	
1530	ethyl	n-butyl	OH	H	
1531	n-butyl	ethyl	OH	H	
1532	n-butyl	n-butyl	OH	H	

1533	ethyl	n-butyl	OH	H	
1534	n-butyl	ethyl	OH	H	
1535	n-butyl	n-butyl	OH	H	
1536	ethyl	n-butyl	OH	H	

1537	n-butyl	ethyl	OH	H	
1538	n-butyl	n-butyl	OH	H	
1539	ethyl	n-butyl	OH	H	
1540	n-butyl	ethyl	OH	H	

1541	n-butyl	n-butyl	OH	H	
1542	ethyl	n-butyl	OH	H	
1543	n-butyl	ethyl	OH	H	
1544	n-butyl	n-butyl	OH	H	

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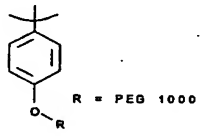
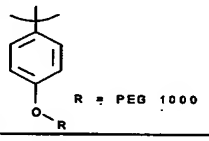
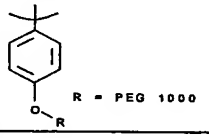
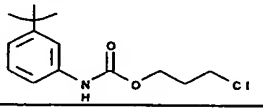
1545	ethyl	n-butyl	OH	H	
1546	n-butyl	ethyl	OH	H	
1547	n-butyl	n-butyl	OH	H	
1548	ethyl	n-butyl	OH	H	

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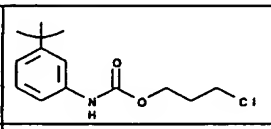
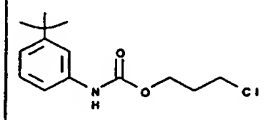
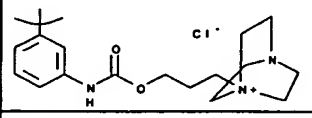
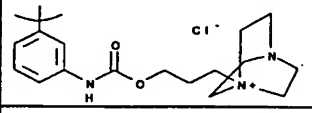
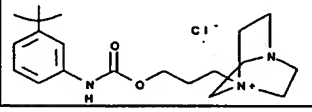
1549	n-butyl	ethyl	OH	H	
1550	n-butyl	n-butyl	OH	H	
1551	ethyl	n-butyl	OH	H	
1552	n-butyl	ethyl	OH	H	
1553	n-butyl	n-butyl	OH	H	

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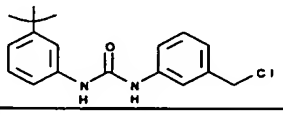
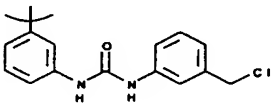
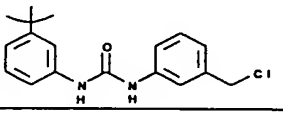
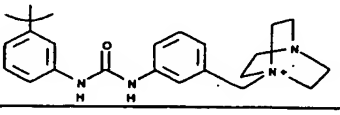
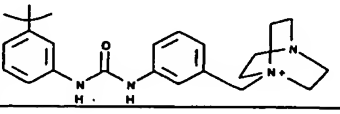
1554	ethyl	n-butyl	OH	H	
1555	n-butyl	ethyl	OH	H	
1556	n-butyl	n-butyl	OH	H	
1557	ethyl	n-butyl	OH	H	
1558	n-butyl	ethyl	OH	H	

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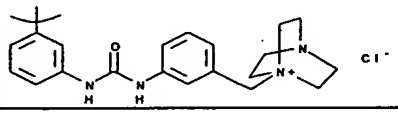
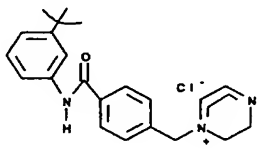
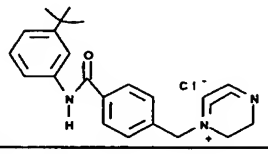
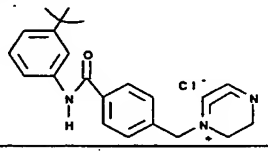
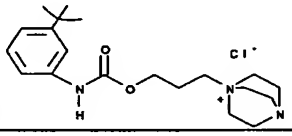
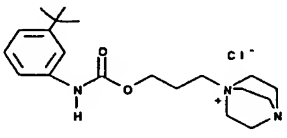
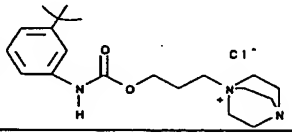
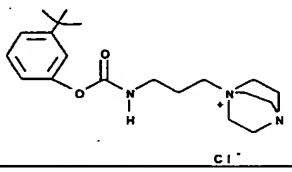
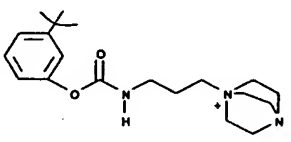
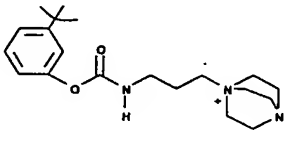
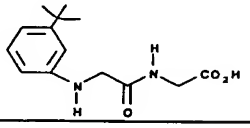
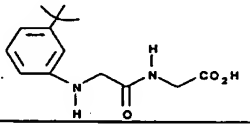
1559	n-butyl	n-butyl	OH	H	
1560	ethyl	n-butyl	OH	H	
1561	n-butyl	n-butyl	OH	H	
1562	n-butyl	n-butyl	OH	H	

1563	ethyl	n-butyl	OH	H	
1564	n-butyl	n-butyl	OH	H	
1565	n-butyl	n-butyl	OH	H	
1566	ethyl	n-butyl	OH	H	

1567	n-butyl	ethyl	OH	H	
1568	n-butyl	n-butyl	OH	H	
1569	ethyl	n-butyl	OH	H	
1570	n-butyl	ethyl	OH	H	

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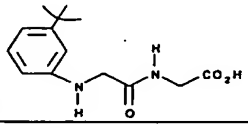
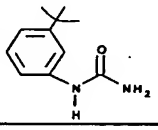
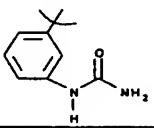
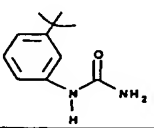
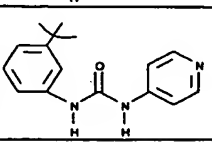
1571	n-butyl	n-butyl	OH	H	
1572	ethyl	n-butyl	OH	H	
1573	n-butyl	ethyl	OH	H	
1574	n-butyl	n-butyl	OH	H	
1575	ethyl	n-butyl	OH	H	

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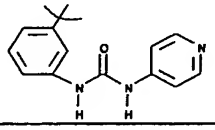
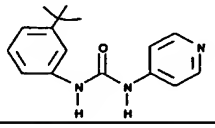
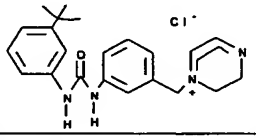
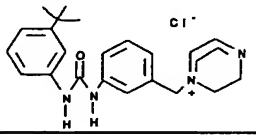
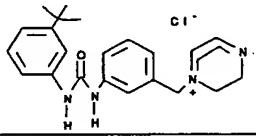
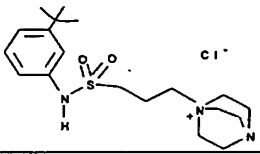
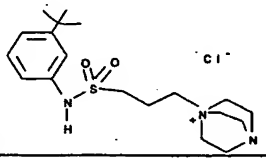
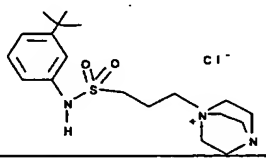
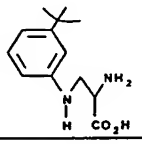
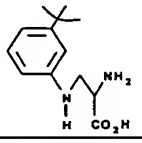
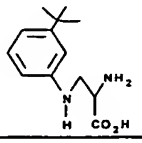
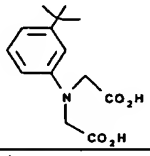
1576	n-butyl	ethyl	OH	H	
1577	n-butyl	n-butyl	OH	H	
1578	ethyl	n-butyl	OH	H	
1579	n-butyl	ethyl	OH	H	

1580	n-butyl	n-butyl	OH	H	
1581	ethyl	n-butyl	OH	H	
1582	n-butyl	ethyl	OH	H	
1583	n-butyl	n-butyl	OH	H	

1584	ethyl	n-butyl	OH	H	
1585	n-butyl	ethyl	OH	H	
1586	n-butyl	n-butyl	OH	H	
1587	ethyl	n-butyl	OH	H	

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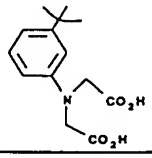
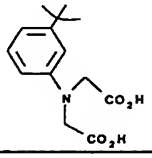
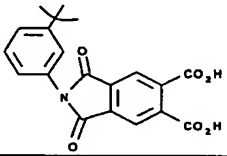
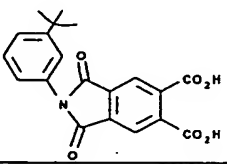
1588	n-butyl	ethyl	OH	H	
1589	n-butyl	n-butyl	OH	H	
1590	ethyl	n-butyl	OH	H	
1591	n-butyl	ethyl	OH	H	

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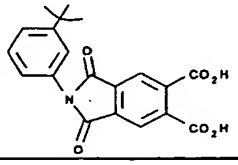
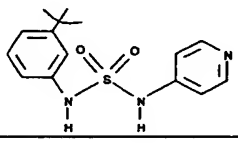
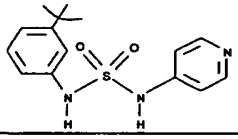
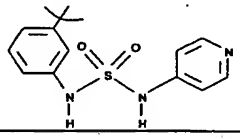
1592	n-butyl	n-butyl	OH	H	
1593	ethyl	n-butyl	OH	H	
1594	n-butyl	n-butyl	OH	H	
1595	n-butyl	n-butyl	OH	H	

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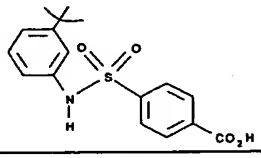
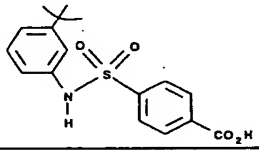
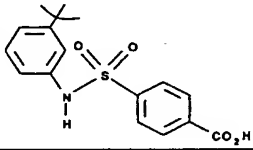
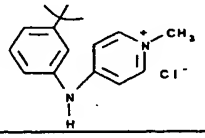
1596	ethyl	n-butyl	OH	H	
1597	n-butyl	ethyl	OH	H	
1598	n-butyl	n-butyl	OH	H	
1599	ethyl	n-butyl	OH	H	

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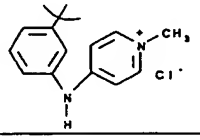
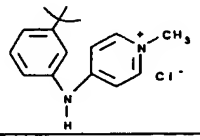
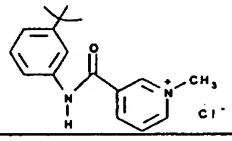
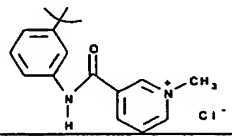
1600	n-butyl	ethyl	OH	H	
1601	n-butyl	n-butyl	OH	H	
1602	ethyl	n-butyl	OH	H	
1603	n-butyl	ethyl	OH	H	

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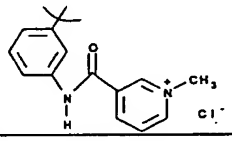
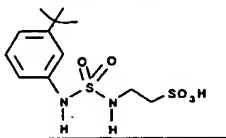
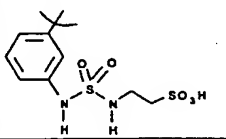
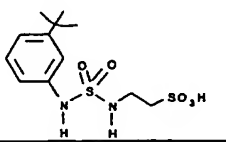
1604	n-butyl	n-butyl	OH	H	
1605	ethyl	n-butyl	OH	H	
1606	n-butyl	ethyl	OH	H	
1607	n-butyl	n-butyl	OH	H	

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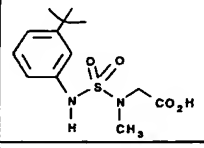
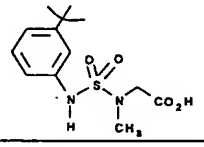
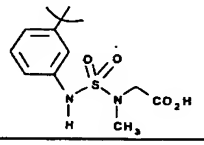
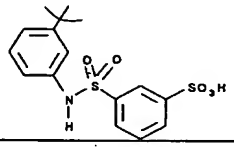
1608	ethyl	n-butyl	OH	H	
1609	n-butyl	ethyl	OH	H	
1610	n-butyl	n-butyl	OH	H	
1611	ethyl	n-butyl	OH	H	

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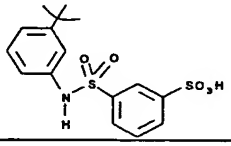
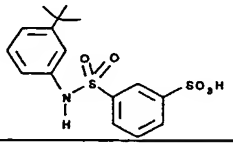
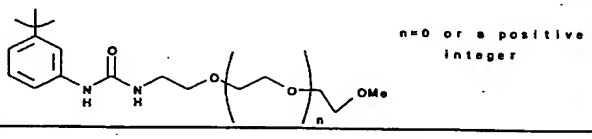
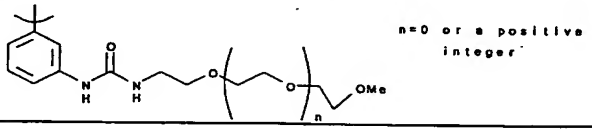
1612	n-butyl	ethyl	OH	H	
1613	n-butyl	n-butyl	OH	H	
1614	ethyl	n-butyl	OH	H	
1615	n-butyl	ethyl	OH	H	

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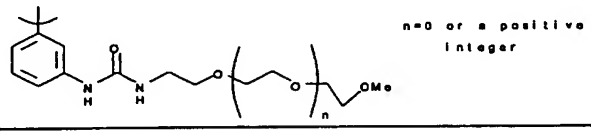
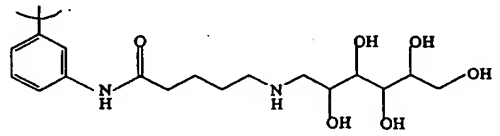
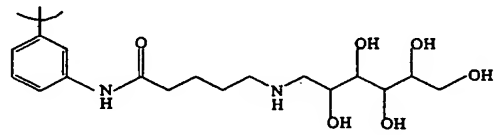
1616	n-butyl	n-butyl	OH	H	
1617	ethyl	n-butyl	OH	H	
1618	n-butyl	ethyl	OH	H	

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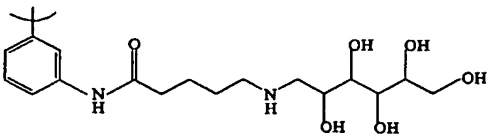
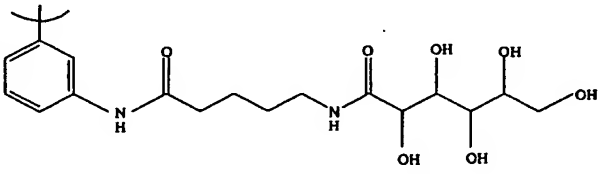
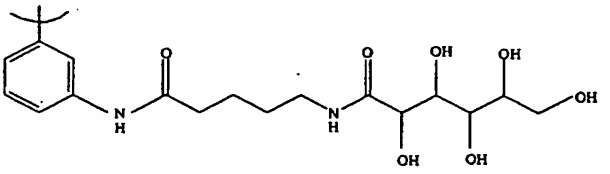
1619	n-butyl	n-butyl	OH	H	
1620	ethyl	n-butyl	OH	H	
1621	n-butyl	ethyl	OH	H	

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1622	n-butyl	n-butyl	OH	H
1623	ethyl	n-butyl	OH	H
1624	n-butyl	ethyl	OH	H

1625	n-butyl	n-butyl	OH	H
1626	ethyl	n-butyl	OH	H
1627	n-butyl	ethyl	OH	H

1628	n-butyl	n-butyl	OH	H
1629	ethyl	n-butyl	OH	H
1630	n-butyl	ethyl	OH	H

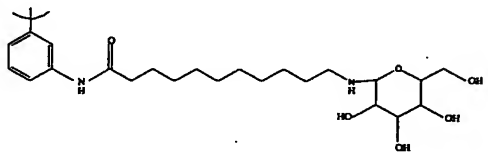
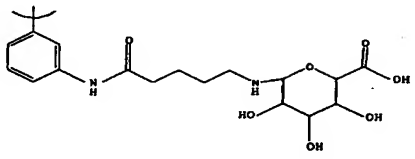
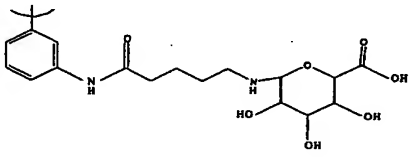
1631	n-butyl	n-butyl	OH	H
1632	ethyl	n-butyl	OH	H
1633	n-butyl	ethyl	OH	H

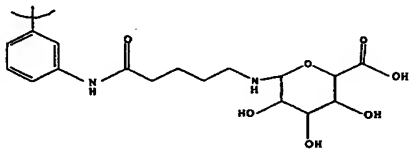
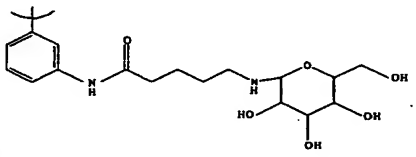
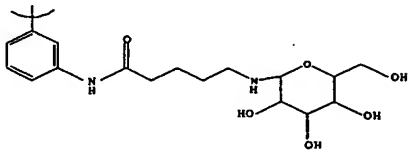
1634	n-butyl	n-butyl	OH	H
1635	ethyl	n-butyl	OH	H
1636	n-butyl	ethyl	OH	H

1637	n-butyl	n-butyl	OH	H
1638	ethyl	n-butyl	OH	H
1639	n-butyl	ethyl	OH	H

1640	n-butyl	n-butyl	OH	H
1641	ethyl	n-butyl	OH	H
1642	n-butyl	ethyl	OH	H

1643	n-butyl	n-butyl	OH	H
1644	ethyl	n-butyl	OH	H
1645	n-butyl	ethyl	OH	H

1646	n-butyl	n-butyl	OH	H	
1647	ethyl	n-butyl	OH	H	
1648	n-butyl	ethyl	OH	H	

1649	n-butyl	n-butyl	OH	H	
1650	ethyl	n-butyl	OH	H	
1651	n-butyl	ethyl	OH	H	

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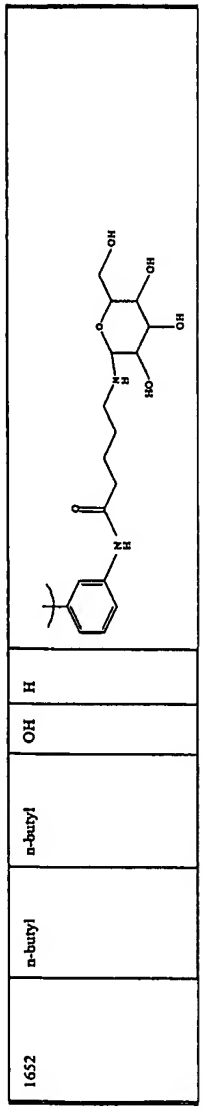

1652	
n-butyl	
n-butyl	
OH	
H	

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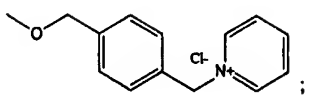
Another group of compounds of interest consists of those compounds of Formula I wherein R^1 and R^2 are alkyl, preferably n-butyl; R^3 is hydroxy; R^4 and R^6 are hydrogen; R^N is hydrogen; R^x radicals are selected from the group consisting of amino, dimethylamino and methoxy; and R^5 is phenyl substituted at the para or meta position with one of the following groups: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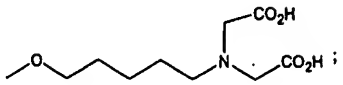
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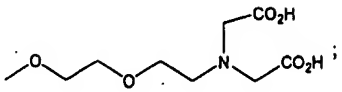
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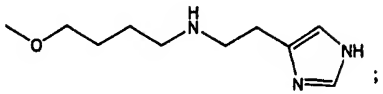
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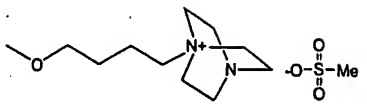
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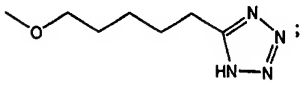
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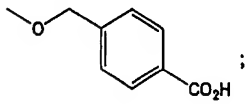
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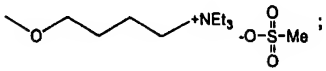
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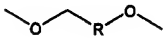
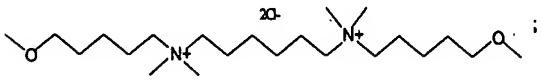

R = 1000 MW PEG ;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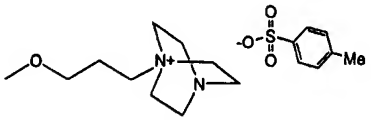
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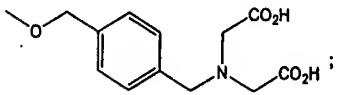
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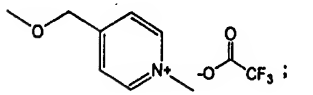
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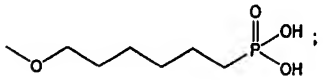
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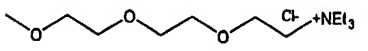
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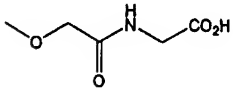
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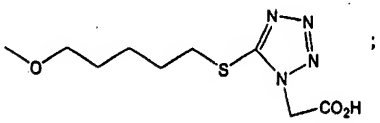
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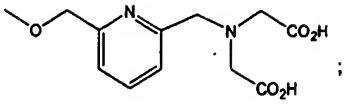
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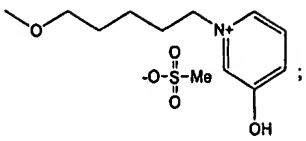
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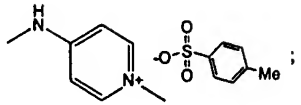
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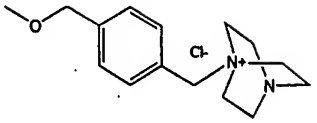
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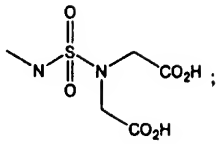
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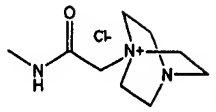
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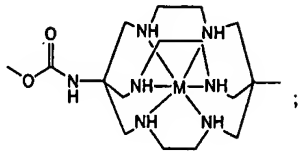

;

wherein M is selected from the group consisting of Co^{II}, Co^{III}, Mn^{II}, Mn^{III}, Fe^{II}, Fe^{III}, Ni^{II}, Ni^{III}, Cr^{III}, Cu^{II}, Zn^{II}, Cd^{II}, Ga^{III}, In^{III}, V^{IV}, Ru^{II}, Pt^{IV}, Rh^{III} and Ir^{III}.

Dosages, Formulations, and Routes of Administration

The ileal bile acid transport inhibitor compounds of the present invention can be administered for the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders by any means, preferably oral, that contacts these compounds with their site of action in the body, for example in the ileum of a mammal such as a human.

For the prophylaxis and/or treatment of the diseases, conditions and/or disorders referred to above, the compounds of the present invention can be used as the compound *per se*. Pharmaceutically acceptable salts are particularly suitable for medical applications because of their greater aqueous solubility relative to the parent compound. Such salts comprise a pharmaceutically acceptable anion or cation. Suitable pharmaceutically

acceptable acid addition salts of the compounds of the present invention where appropriate include those salts derived from inorganic acids, such as hydrochloric, hydrobromic, phosphoric, metaphosphoric, nitric, sulfonic, and sulfuric acids, and organic acids such as acetic, benzenesulfonic, benzoic, citric, ethanesulfonic, fumaric, gluconic, glycolic, isothionic, lactic, lactobionic, maleic, malic, methanesulfonic, succinic, toluenesulfonic, tartaric, and trifluoroacetic acids. The chloride salt is particularly preferred for medical purposes. Suitable pharmaceutically acceptable base salts where appropriate include ammonium salts, alkali metal salts such as sodium and potassium salts, and alkaline earth salts such as magnesium and calcium salts.

The anions of the definition of A^- in the present invention are pharmaceutically acceptable anions such as those anions selected, for example, from the above list.

The compounds of the present invention also can be administered in the form of a pharmaceutical composition comprising additional ingredients such as acceptable carriers, diluents, excipients, adjuvants and the like (collectively referred to herein as "carrier materials"). Acceptable carrier materials are compatible with the other ingredients of the composition and are not deleterious to the recipient. A carrier material can be a solid or a liquid, or both, and is preferably formulated with the compound as a unit-dose composition, for example, a tablet or capsule, which can contain from 0.05% to 95% by weight of the active compound. Other pharmacologically active substances can also be present, including other compounds of the present invention. The pharmaceutical compositions of the invention can be prepared by any of the well known techniques of pharmacy, consisting essentially of admixing the components.

These compounds can be administered by any conventional means available for use in conjunction with pharmaceuticals, either as an individual therapeutic compound in a monotherapeutic regimen or as a combination of

therapeutic compounds in a combination therapy regimen.

The amount of compound that is required to achieve the desired biological effect will depend on a number of factors such as the specific compound chosen, the use for which it is intended, the mode of administration, and the clinical condition of the recipient.

In general, a daily dose can be in the range of from about 0.3 to about 100 mg/kg bodyweight/day, preferably from about 1 mg to about 50 mg/kg bodyweight/day, and more preferably from about 3 to about 10 mg/kg bodyweight/day. This total daily dose can be administered to the patient in a single dose, or in proportionate multiple subdoses. Subdoses can be administered 2 to 6 times per day. Doses can be in sustained release form effective to obtain desired results.

Orally administrable unit dose formulations, such as tablets or capsules, can contain, for example, from about 0.1 to about 100 mg of benzothiazepine compound, preferably about 1 to about 75 mg of compound, more preferably from about 10 to about 50 mg of compound. In the case of pharmaceutically acceptable salts, the weights indicated above refer to the weight of the benzothiazepine ion derived from the salt.

Oral delivery of an ileal bile acid transport inhibitor of the present invention can include formulations, as are well known in the art, to provide prolonged or sustained delivery of the drug to the gastrointestinal tract by any number of mechanisms. These include, but are not limited to, pH sensitive release from the dosage form based on the changing pH of the small intestine, slow erosion of a tablet or capsule, retention in the stomach based on the physical properties of the formulation, bioadhesion of the dosage form to the mucosal lining of the intestinal tract, or enzymatic release of the active drug from the dosage form. The intended effect is to extend the time period over which the active drug molecule is delivered to the site of action (the ileum) by manipulation of the dosage form. Thus, enteric-coated and enteric-coated

controlled release formulations are within the scope of the present invention. Suitable enteric coatings include cellulose acetate phthalate, polyvinylacetate phthalate, hydroxypropylmethylcellulose phthalate and anionic polymers of methacrylic acid and methacrylic acid methyl ester.

When administered intravenously, the dose can, for example, be in the range of from about 0.1 mg/kg body weight to about 1.0 mg/kg body weight, preferably from about 0.25 mg/kg body weight to about 0.75 mg/kg body weight, and more preferably from about 0.4 mg/kg body weight to about 0.6 mg/kg body weight. This dose can be conveniently administered as an infusion of from about 10 ng/kg body weight to about 100 ng/kg body weight per minute. Infusion fluids suitable for this purpose can contain, for example, from about 0.1 ng to about 10 mg, and preferably from about 1 ng to about 10 mg per milliliter. Unit doses can contain, for example, from about 1 mg to about 10 g of the compound of the present invention. Thus, ampoules for injection can contain, for example, from about 1 mg to about 100 mg.

Pharmaceutical compositions according to the present invention include those suitable for oral, rectal, topical, buccal (e.g., sublingual), and parenteral (e.g., subcutaneous, intramuscular, intradermal, or intravenous) administration, although the most suitable route in any given case will depend on the nature and severity of the condition being treated and on the nature of the particular compound which is being used. In most cases, the preferred route of administration is oral.

Pharmaceutical compositions suitable for oral administration can be presented in discrete units, such as capsules, cachets, lozenges, or tablets, each containing a predetermined amount of at least one compound of the present invention; as a powder or granules; as a solution or a suspension in an aqueous or non-aqueous liquid; or as an oil-in-water or water-in-oil emulsion. As indicated, such compositions can be prepared by any suitable method of pharmacy which includes the step of bringing into association the active

compound(s) and the carrier material (which can constitute one or more accessory ingredients). In general, the compositions are prepared by uniformly and intimately admixing the active compound with a liquid or finely divided solid carrier material, or both, and then, if necessary, shaping the product. For example, a tablet can be prepared by compressing or molding a powder or granules of the compound, optionally with one or more assessory ingredients. Compressed tablets can be prepared by compressing, in a suitable machine, the compound in a free-flowing form, such as a powder or granules optionally mixed with a binder, lubricant, inert diluent and/or surface active/dispersing agent(s). Molded tablets can be made by molding, in a suitable machine, the powdered compound moistened with an inert liquid diluent.

Pharmaceutical compositions suitable for buccal (sub-lingual) administration include lozenges comprising a compound of the present invention in a flavored base, usually sucrose, and acacia or tragacanth, and pastilles comprising the compound in an inert base such as gelatin and glycerin or sucrose and acacia.

Pharmaceutical compositions suitable for parenteral administration conveniently comprise sterile aqueous preparations of a compound of the present invention. These preparations are preferably administered intravenously, although administration can also be effected by means of subcutaneous, intramuscular, or intradermal injection. Such preparations can conveniently be prepared by admixing the compound with water and rendering the resulting solution sterile and isotonic with the blood. Injectable compositions according to the invention will generally contain from 0.1 to 5% w/w of a compound disclosed herein.

Pharmaceutical compositions suitable for rectal administration are preferably presented as unit-dose suppositories. These can be prepared by admixing a compound of the present invention with one or more conventional

solid carrier materials, for example, cocoa butter, and then shaping the resulting mixture.

Pharmaceutical compositions suitable for topical application to the skin preferably take the form of an ointment, cream, lotion, paste, gel, spray, aerosol, or oil. Carrier materials that can be used include vaseline, lanoline, polyethylene glycols, alcohols, and combinations of two or more thereof. The active compound is generally present at a concentration of from 0.1 to 15% w/w of the composition, for example, from 0.5 to 2%.

Transdermal administration is also possible. Pharmaceutical compositions suitable for transdermal administration can be presented as discrete patches adapted to remain in intimate contact with the epidermis of the recipient for a prolonged period of time. Such patches suitably contain a compound of the present invention in an optionally buffered, aqueous solution, dissolved and/or dispersed in an adhesive, or dispersed in a polymer. A suitable concentration of the active compound is about 1% to 35%, preferably about 3% to 15%. As one particular possibility, the compound can be delivered from the patch by electrotransport or iontophoresis, for example, as described in Pharmaceutical Research, 3(6), 318 (1986).

In any case, the amount of active ingredient that can be combined with the carrier materials to produce a single dosage form to be administered will vary depending upon the host treated and the particular mode of administration.

The solid dosage forms for oral administration including capsules, tablets, pills, powders, and granules noted above comprise one or more compounds of the present invention admixed with at least one inert diluent such as sucrose, lactose, or starch. Such dosage forms may also comprise, as in normal practice, additional substances other than inert diluents, e.g., lubricating agents such as magnesium stearate. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents. Tablets and

pills can additionally be prepared with enteric coatings.

Liquid dosage forms for oral administration can include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs containing inert diluents commonly used in the art, such as water. Such compositions may also comprise adjuvants, such as wetting agents, emulsifying and suspending agents, and sweetening, flavoring, and perfuming agents.

Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions may be formulated according to the known art using suitable dispersing or setting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

Pharmaceutically acceptable carrier materials encompass all the foregoing and the like.

Treatment Regimen

The dosage regimen to prevent, give relief from, or ameliorate a disease, condition and/or disorder relating to hyperlipemia, e.g., atherosclerosis, or to protect against or treat further high cholesterol plasma or blood levels with the compounds and/or compositions of the present invention is selected in accordance with a variety of factors. These include the type, age, weight, sex, diet, and medical condition of the patient, the severity of the disease, the route of administration, pharmacological considerations such as

the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized, and whether the compound is administered as part of a drug combination. Thus, the dosage regimen actually employed may vary widely and therefore deviate from the preferred dosage regimen set forth above.

Initial treatment of a patient suffering from a hyperlipidemic condition can begin with the dosages indicated above. Treatment should generally be continued as necessary over a period of several weeks to several months or years until the hyperlipidemic disease condition has been controlled or eliminated. Patients undergoing treatment with the compounds or compositions disclosed herein can be routinely monitored by, for example, measuring serum cholesterol levels by any of the methods well known in the art, to determine the effectiveness of therapy. Continuous analysis of such data permits modification of the treatment regimen during therapy so that optimal effective amounts of compounds of the present invention are administered at any point in time, and so that the duration of treatment can be determined as well. In this way, the treatment regimen/dosing schedule can be rationally modified over the course of therapy so that the lowest amount of ileal bile acid transport inhibitor of the present invention which exhibits satisfactory effectiveness is administered, and so that administration is continued only so long as is necessary to successfully treat the hyperlipidemic condition.

The following non-limiting examples serve to illustrate various aspects of the present invention.

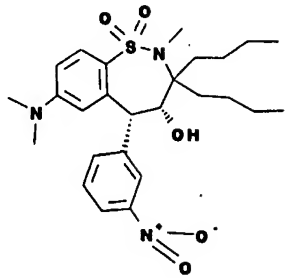
Examples of Synthetic Procedures

The starting materials used in the preparation of the compounds of the following examples, as well as other compounds of the present invention, are commercially available or can be prepared by conventional methods known to one of ordinary skill in the art or in an analogous manner to conventional

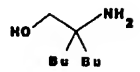
methods described in the art. The starting materials of the following examples were obtained from commercial sources unless otherwise noted. The ethyl 2-amino-2-butylhexanoate hydrochloride used below was prepared in an analogous manner to the literature method of Stork (*J. Org. Chem.* 41, 3491 (1976)).

Example 1

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide



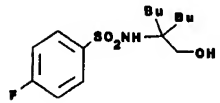
Step 1. 2-Amino-2-butylhexanol



To a solution of 29.75 g (0.12 mol) of ethyl 2-amino-2-butylhexanoate hydrochloride in 100 mL of tetrahydrofuran cooled to -20 °C was added 148.8 mL of a 1.0 M solution of lithium aluminum hydride in tetrahydrofuran while

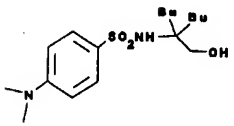
maintaining a temperature below -15 °C. The reaction mixture was stirred for one hour at -20 °C, warmed to room temperature and stirred for 16 hours. The reaction mixture was then cooled to -20 °C and 6 mL of water was added, followed by 5.6 mL of 3.75 M aqueous sodium hydroxide and 16 mL of water. The reaction mixture was stirred for one hour and warmed to room temperature. The resulting slurry was filtered and washed with 100 mL ethyl acetate. The ethyl acetate solution was washed with water (2x200 mL) and then brine (300 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated. The resulting yellow oil was dissolved in 300 mL of tetrahydrofuran and concentrated to give 20.61 g of 2-amino-2-butylhexanol as an oil.

Step 2. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-fluorobenzenesulfonamide



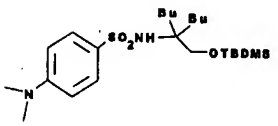
To a solution of 16.95 g (0.09 mol) of 4-fluorobenzene sulfonyl chloride in 150 mL of tetrahydrofuran was added 36.4 mL of triethylamine. The reaction mixture was cooled to 0 °C and a solution of 19.61 g of 2-amino-2-butylhexanol (prepared in step 1 above) in 70 mL of tetrahydrofuran was added. The reaction mixture was stirred 30 minutes at 0 °C and then 16 hours at room temperature. The reaction mixture was concentrated and then the residue was dissolved in 250 mL of ethyl acetate. This ethyl acetate solution was washed with water (2 x 200 mL) and brine (300 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 29.47 g of *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-fluorobenzenesulfonamide as an oil.

Step 3. *N*-(1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino) benzenesulfonamide



A solution containing 28.89 g (0.09 mol) of the oil prepared in Step 2 above, 872 mL of 2.0 M dimethylamine in tetrahydrofuran and 100 mL of neat dimethylamine was prepared and placed in a bomb. The reaction mixture was heated to 110 °C for 16 hours, cooled, and then concentrated to give 25.46 g of *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)benzenesulfonamide as an solid.

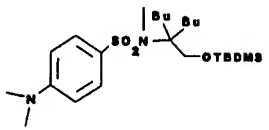
Step 4. *N*-[1-Butyl-1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)benzenesulfonamide



To a solution of 15.51 g (0.10 mol) of *t*-butyldimethylsilyl chloride in 158 mL of dimethylformamide was added 24.46 g (0.07 mol) of the solid prepared in Step 3 and then 14.01 g of imidazole. The reaction mixture was stirred 3 days and then diluted with 1 L of ethyl acetate and 500 mL of water. The ethyl acetate solution was washed with 5% hydrochloric acid solution (2 x

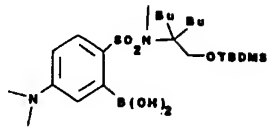
200 mL), water (200 mL) and then brine (200 mL). The ethyl acetate layer was dried with magnesium sulfate and concentrated to an oil. The oil was stirred with hexane and the resulting solid was filtered to give 25.31 g of *N*-[1-butyl-1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)benzenesulfonamide as a white solid.

Step 5. *N*-[1-Butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-*N*-methylbenzenesulfonamide



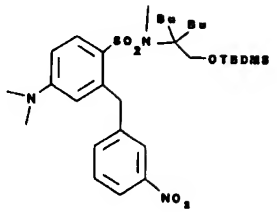
To a solution of 0.476 g (11.90 mmol) of 60% sodium hydride dispersion in mineral oil in 43 mL of tetrahydrofuran was added 4.0 g (8.50 mmol) of the solid prepared in Step 4 above and then 1.6 mL of dimethyl sulfate dropwise. The reaction mixture was heated at reflux for one hour, cooled to 0 °C, and then water was added. The reaction mixture was concentrated and 250 mL ethyl acetate and 250 mL water added. The layers were separated and the ethyl acetate solution was washed with 1 M hydrochloric acid (2 x 200 mL), saturated sodium bicarbonate (2 x 200 mL), water (200 mL) and then brine (200 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 4.63 g of a residue. The residue was purified by flash chromatography with 15% ethyl acetate/hexane as eluent to give 3.35 g of *N*-[1-butyl-1-[[[(1,1dimethylethyl) dimethylsilyl] oxy]methyl]pentyl]-4-(dimethylamino)-*N*-methylbenzenesulfonamide as an oil.

Step 6.



To a solution of 3.35 g (6.90 mmol) of the oil prepared in Step 5 above in 35 mL of tetrahydrofuran cooled to 0 °C was added dropwise 9.66 mL of 1.6 M *n*-butyllithium in hexanes. The reaction mixture was stirred 30 minutes at 0 °C, warmed to room temperature, and stirred one hour. To the reaction mixture was added 6.5 mL of 5% hydrochloric acid and then the Tetrahydrofuran was evaporated. To the residue was added 200 mL dichloromethane and 200 mL water and the layers separated. The dichloromethane layer was washed with brine (200 mL), dried over magnesium sulfate and concentrated to give 3.12 g of a yellow solid.

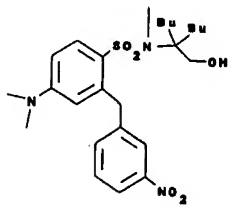
Step 7. *N*-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide



To a solution of 130 mg (0.11 mmol) of tetrakis(triphenylphosphine) palladium(0) in 10 mL of toluene was added 825 mg of 3-nitrobenzyl

bromide. After the toluene solution was stirred 10 minutes, a degassed solution of 2.02 g (3.82 mmol) of the solid prepared in Step 6 above in 8 mL ethanol was added followed by 10 mL of 1 M sodium carbonate. The reaction mixture was heated at reflux 45 minutes and then cooled and concentrated. To the residue was added 250 mL of ethyl acetate. The ethyl acetate mixture was washed with brine (2 x 200 mL), dried over magnesium sulfate and concentrated to give 2.76 g of a residue. To the residue was added 200 mL of 30% ethyl acetate in hexane, and the mixture was stirred 1.5 hours and then filtered through silica. The ethyl acetate solution was concentrated to give 2.30 g of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide as a yellow solid.

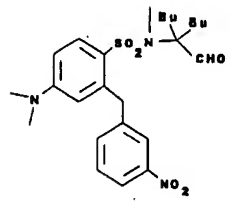
Step 8. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide



To a solution of 2.16 g (3.48 mmol) of the solid prepared in Step 7 above in 10 mL of tetrahydrofuran cooled to 0 °C was added 4.4 mL of 1 M tetrabutylammonium fluoride in tetrahydrofuran. The reaction mixture was stirred 15 minutes at 0 °C and then 12 hours at room temperature. To the reaction mixture was added 250 mL of ethyl acetate. The ethyl acetate solution was washed with water (200 mL) and brine (200 mL). The ethyl

acetate layer was dried over magnesium sulfate and concentrated to give 1.88 g of a brown oil residue. The residue was purified by flash chromatography with 30% ethyl acetate in hexane as eluent to give 1.49 g of *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide as a yellow oil.

Step 9. *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.



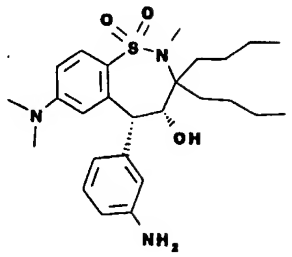
To a solution of 1.49 g (2.95 mmol) of the oil prepared in Step 8 above in 10 mL of dimethylsulfoxide was added 1.23 mL of triethylamine and then 1.41 g of sulfur trioxide pyridine complex. The reaction mixture was stirred one hour and then diluted with 200 mL water. The aqueous mixture was washed with ethyl acetate (3 x 100 mL). The combined organic layers were washed with 5% hydrochloric acid (100 mL) and brine (100 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated. The residue was purified by flash chromatography with 25% ethyl acetate in hexane as eluent to give 1.31 g of *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide as a yellow oil.

Step 10. (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

To a solution of 504 mg (2.60 mmol) of the oil prepared in Step 9 above in 50 mL of tetrahydrofuran cooled to 0 °C was added 2.80 mL of 1 M potassium *t*-butoxide in tetrahydrofuran. The reaction mixture was stirred for 15 minutes, water was added, and then the mixture was concentrated to yield a residue. The residue was dissolved in 100 mL ethyl acetate. The ethyl acetate solution was washed with water (100 mL) and brine (100 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 1.25 g of a semi-solid. The residue was purified by crystallization with ethyl acetate and hexane to give 737.5 mg of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide as a yellow crystalline solid. ^{1}H NMR ($CDCl_3$) δ 0.90-1.00 (m, 6H), 1.05-1.80 (m, 12H), 2.50-2.60 (m, 1H), 2.79 (s, 6H), 2.85 (s, 3H), 4.09 (d, *J* = 9.0 Hz, 1H), 5.76 (d, *J* = 2.0 Hz, 1H), 5.88 (s, 1H), 6.53 (dd, *J* = 2.4, 8.9 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.84-7.88 (m, 2H), 8.22 (dd, *J* = 1.0, 8.1 Hz, 1H), 8.47 (s, 1H). MS (M+H$^+$) 504.

Example 2

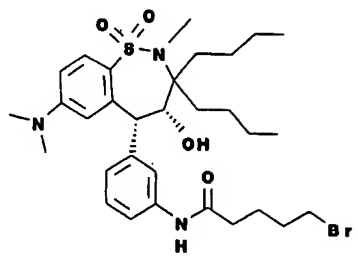
(4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide



A solution of 737 mg (1.46 mmol) of the solid prepared in Step 10 of Example 1 was dissolved in 110 mL of ethanol in a 3 oz. Fisher/Porter vessel, and about 150 mg of 10% Pd/C catalyst was added. This mixture was hydrogenated at 40 psi H_2 for 20 hours and then filtered. The filtrate was concentrated to give 0.82 g of a semi-solid material. The semi-solid material was crystallized from ethyl acetate and hexane to give 0.51 g of (4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide as colorless crystals. ^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 6.6 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H), 1.10-1.45 (m, 8H), 1.60-1.75 (m, 3H), 1.98-2.10 (m, 1H), 2.48-2.58 (m, 1H), 2.79 (s, 6H), 2.81 (s, 3H), 3.69 (s, 2H), 4.12 (d, *J* = 7.8 Hz, 1H), 5.62 (s, 1H), 6.07 (d, *J* = 2.1 Hz, 1H), 6.46 (dd, *J* = 2.4, 8.7 Hz, 1H), 6.61 (br d, *J* = 7.8 Hz, 1H), 6.80 (br s, 1H), 6.89 (br d, *J* = 2.1 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 8.7 Hz, 1H). MS (M+H$^+$) 474.

Example 3

5-bromo-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]pentanamide

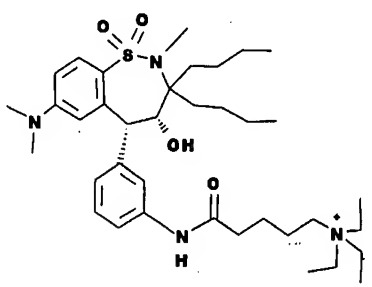


To a solution of 0.25 g (0.53 mmol) of the solid prepared in Example 2

above in 3 mL of tetrahydrofuran was added 153 µL of triethylamine followed by 86 µL of 5-bromovaleryl chloride. The reaction mixture was stirred one hour and then concentrated to form a residue. Water (50 mL) was added to the residue. The aqueous solution was extracted with ethyl acetate (2 x 50 mL). The combined ethyl acetate layers were washed with 5% hydrochloric acid (2 x 25 mL), saturated sodium bicarbonate solution (2 x 25 mL) and brine (25 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 0.29 g of a solid. The solid was purified by crystallization with ethyl acetate and hexane to give 202.3 mg of 5-bromo-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]pentanamide as a tan solid. ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 6.9 Hz, 3H), 1.20-1.42 (m, 8H), 1.57-2.10 (m, 8H), 2.37 (t, *J* = 6.9 Hz, 2H), 2.46-2.57 (m, 1H), 2.78 (s, 6H), 2.81 (m, 3H), 3.41 (t, *J* = 6.3 Hz, 2H), 4.10 (d, *J* = 8.5 Hz, 1H), 5.69 (s, 1H), 5.97 (s, 1H), 6.47 (dd, *J* = 2.4, 8.9 Hz, 1H), 7.24-7.40 (m, 4H), 7.76 (br s, 1H), 7.80 (d, *J* = 8.7 Hz, 1H). MS ($M+H^+$) 636, 638.

Example 4

5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N*,*N*,*N*-triethyl-5-oxo-pentanaminium trifluoroacetate

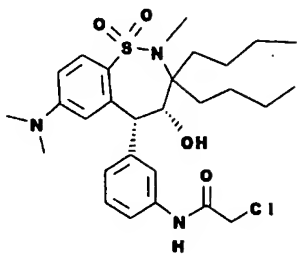


$CF_3CO_2^-$

To a solution of 100 mg (0.16 mmol) of the solid prepared in Example 3 above in 1 mL of acetonitrile was added 87 µL of triethylamine. The reaction mixture was heated at 55 °C for 28 hours and then at 75 °C for 16 hours. The reaction mixture was concentrated to form a residue. The residue was purified by reverse phase high pressure liquid chromatography to give 16.2 mg of 5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N*,*N*,*N*-triethyl-5-oxo-pentanaminium trifluoroacetate as a white solid. ^{1}H NMR was consistent with the product. MS (M^+) 657.

Example 5

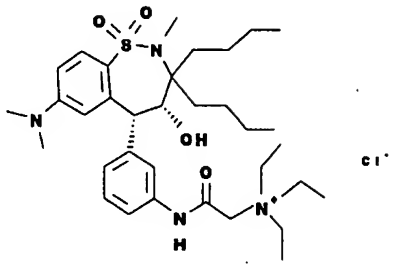
2-chloro-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]acetamide



To a solution of 100 mg (0.21 mmol) of the solid prepared in Example 4 above in 2 mL of tetrahydrofuran was added 29 mg of bromoacetic acid, 29 µL of triethylamine, and then 40 mg of ethyldimethylaminopropylcarbodiimide hydrochloride. The reaction mixture was stirred 16 hours and then 50 mL ethyl acetate was added. The ethyl acetate solution was washed with water, 5% hydrochloric acid (2 x 25 mL), saturated sodium bicarbonate solution (2 x 25 mL), and then brine (25 mL). The ethyl acetate layer was dried over magnesium sulfate and then concentrated to give 88 mg of an oil. The oil was purified by flash chromatography with 50% ethyl acetate in hexane as eluent to give 72.0 mg of *cis*-3,3-dibutyl-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-7-dimethylamino-5-(3-(2-chloroaceamido)phenyl)-1,2-benzothiazepine with a trace of 2-chloro-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]acetamide present. ^{1}H NMR was consistent with the product. MS (M+H$^+$) 550.

Example 6

2-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-2-oxoethanaminium chloride



To a mixture of 63 mg (0.12 mmol) of the material prepared in Example 5 above in 1 mL of tetrahydrofuran was added 64 µL of triethylamine. The reaction mixture was heated to reflux for three days and then concentrated. The residue was triturated with ether to give 66.5 mg of 2-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-2-oxoethanaminium chloride as a tan solid. ^{1}H NMR was consistent with the product. MS (M$^+$) 615.

Example 7

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

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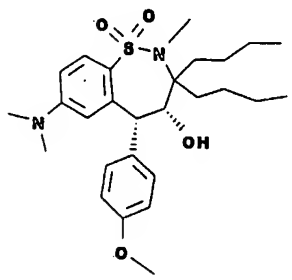
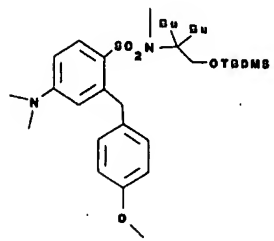


Step 1. *N*-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide



To a solution of 1.00 g (2.06 mmol) of the material from Step 5 of Example 1 above in 10 mL of tetrahydrofuran cooled to 0 °C was added 2 mL of 1.6 M *n*-butyllithium in hexanes. The reaction mixture was stirred one hour at 0 °C. To the reaction mixture was added 480 µL of trimethyl borate and the mixture stirred 15 minutes at 0 °C and then one hour at room temperature. The reaction mixture was concentrated to form a residue. The residue was dissolved in 20 mL of toluene and 2.1 mL of 2 M aqueous sodium carbonate.

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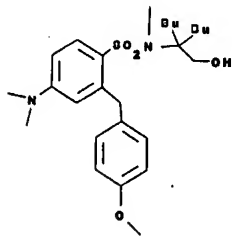
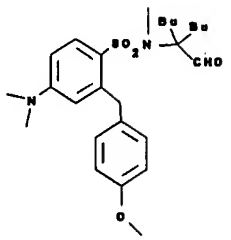
To the mixture was added 300 µL of *p*-methoxybenzyl chloride and then 71 mg of tetrakis(triphenylphosphine)palladium(0). The reaction mixture was heated at 100 °C for 16 hours, cooled, and then 50 mL of toluene added. The reaction mixture was washed with water (50 mL) and brine (50 mL), filtered through silica, and concentrated to form a residue. The residue was purified by flash chromatography to give 0.82 g of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide as an oil.

Step 2. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide



The procedure of Step 8 of Example 1 above was followed except that *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

Step 3. *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl) methyl]-*N*-methylbenzenesulfonamide



The procedure of Step 9 of Example 1 above was followed except that *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide was used in place of *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

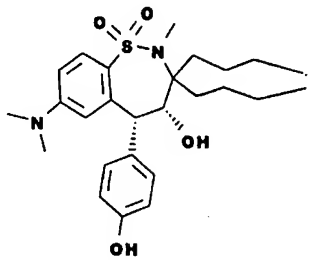
Step 4. (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

The procedure of Step 10 of Example 1 above was followed except that *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide was used in place of *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

^{1}H NMR ($CDCl_3$) δ 0.83-0.96 (m, 6H), 1.15-1.38 (m, 6H), 1.69-1.83 (m, 4H), 2.00-2.08 (m, 1H), 2.55-2.59 (m, 1H), 2.81 (s, 6H), 2.83 (s, 3H), 3.84 (s, 3H), 4.10-41.6 (m, 1H), 5.70 (s, 1H), 5.99 (s, 1H), 6.52 (s, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.6 Hz).

Example 8

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

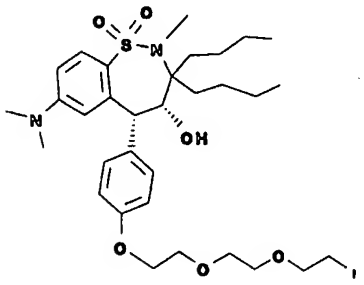


To a solution of 0.52 g (1.06 mmol) of the solid prepared in Step 4 of Example 7 above in 10 mL of dichloromethane cooled to -78 °C was added 300 µL of boron tribromide. The reaction mixture was stirred for one hour at -78 °C and then 100 mL of water and 100 mL of dichloromethane were added. The dichloromethane solution was washed with 10% aqueous sodium carbonate(100 mL), 10% hydrochloric acid (100 mL) and brine (100 mL). The dichloromethane layer was dried over magnesium sulfate and concentrated to give 0.46 g of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide as a solid. ^{1}H NMR ($CDCl_3$) δ 0.82-0.97 (m, 6H), 1.15-1.40 (m, 6H), 1.67-1.76 (m, 4H), 2.00-2.10 (m, 1H), 2.51-2.59 (m, 1H), 2.83 (s, 6H), 2.84 (s, 9H), 4.12 (d, *J* = 8.0 Hz, 1H), 4.88 (br s, 1H), 5.69 (s, 1H), 6.07 (d, *J* = 2.2 Hz, 1H), 6.60 (dd, *J* = 2.2, 8.6 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.85 (d, *J* = 8.6 Hz). HRMS (ES) Calc'd for $C_{26}H_{39}N_2O_4S$: 475.2631.

Found: 475.2649.

Example 9

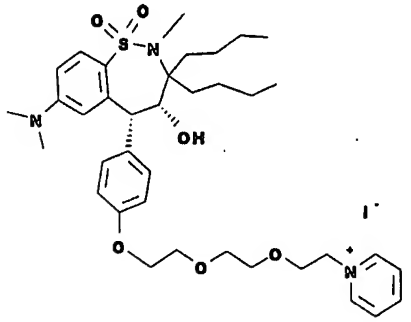
(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide



To a solution of 0.38 g (0.80 mmol) of the solid prepared in Example 8 in 8 mL dimethylformamide was added 44 mg of 95% sodium hydride and then 730 µL of 1,2-bis(2-iodoethoxy)ethane. The reaction mixture was stirred one hour. To the reaction mixture was added 100 mL of water and 100 mL of ethyl acetate and the reaction mixture extracted with ethyl acetate. The ethyl acetate layer was washed with brine (100 mL), dried over magnesium sulfate and concentrated to form a residue. The residue was purified by flash chromatography with 10-25% ethyl acetate in hexane as eluent to give 0.37 g of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide as a solid. HRMS (ES) Calc'd for $C_{32}H_{50}N_1O_6SI$: 717.2434. Found: 717.2419. ^1H NMR is consistent with the structure of the product.

Example 10

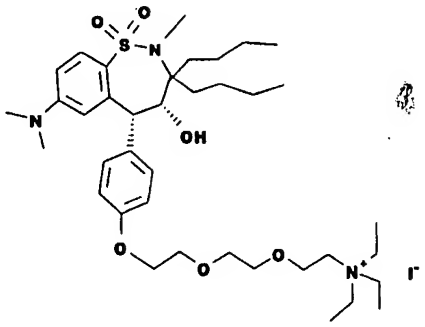
1-[2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]ethyl]pyridinium



A solution of 75 mg of the solid prepared in Example 9 above in 5 mL of pyridine was heated at 70 °C for 16 hours. The reaction mixture was concentrated to form a residue. The residue was triturated with ether to give 56.8 mg of 1-[2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]ethyl]pyridinium as a solid. ^1H NMR ($CDCl_3$) δ 0.89-0.97 (m, 6H), 1.19-1.40 (m, 6H), 1.70-1.74 (m, 4H), 2.00-2.10 (m, 1H), 2.60-2.69 (m, 1H), 2.80 (s, 6H), 2.83 (s, 3H), 3.69-3.72 (m, 4H), 3.83-3.87 (m, 2H), 4.09-4.15 (m, 5H), 5.23-5.27 (m, 2H), 5.70 (s, 1H), 5.97 (d, J = 2.4 Hz, 1H), 6.50 (dd, J = 2.4, 8.8 Hz, 1H), 6.93 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.7 Hz, 2H), 7.83 (d, J = 8.7 Hz, 1H), 7.96-8.01 (m, 2H), 8.63-8.67 (m, 2H), 9.52 (d, J = 6.0 Hz, 1H). HRMS (ES) Calc'd for $C_{37}H_{54}N_3O_6S$: 668.3733. Found: 668.3762.

Example 11

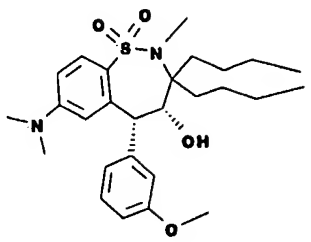
2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-*N*,*N*,*N*-triethylethanaminium iodide



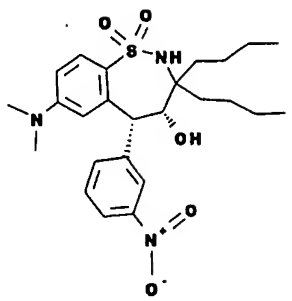
The procedure of Example 10 was followed except that triethylamine was used in place of pyridine and heating was at 90 °C for 6 hours. ^{1}H NMR is consistent with the desired product. ^{1}H NMR ($CDCl_3$) δ 0.90-0.97 (m, 6H), 1.12-1.45 (m, 15H), 1.60-1.73 (m, 4H), 2.09-2.11 (m, 1H), 2.52-2.55 (m, 1H), 2.82 (s, 6H), 2.83 (s, 3H), 3.06-3.15 (m, 2H), 3.53 (q, *J* = 7.2 Hz, 6H), 3.74-3.75 (m, 4H), 3.86-3.89 (m, 2H), 4.04-4.16 (m, 5H), 5.70 (s, 1H), 5.98 (m, 1H), 6.50 (d, *J* = 3.0 Hz, 1H), 6.93 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.83 (d, *J* = 8.7 Hz, 1H). HRMS (ES) Calc'd for $C_{38}H_{64}N_3O_6S$: 690.4516. Found: 690.4548.

Example 12

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide

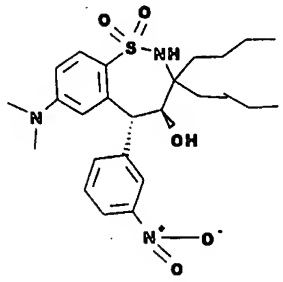


The procedures set forth in Example 1 above were followed except that 3-methoxybenzyl chloride was substituted for 3-nitrobenzyl chloride. ^{1}H NMR was consistent with the product. ^{1}H NMR ($CDCl_3$) δ 0.90-0.97 (m, 6H), 1.17-1.38 (m, 8H),1.69-1.73 (m, 2H), 2.04-2.08 (m, 1H), 2.55-2.62 (m, 1H), 2.81 (s, 6H), 2.84 (s, 3H), 3.82 (s, 3H), 4.15 (d, *J* = 7.8 Hz, 1H), 5.72 (s, 1H), 6.01 (d, *J* = 2.4 Hz, 1H), 6.50 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.86-6.89 (m, 1H), 7.05 (br s, 1H), 7.13-7.16 (m, 1H), 7.32 (t, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 8.7 Hz, 1H). MS (M+H$^+$) 489.

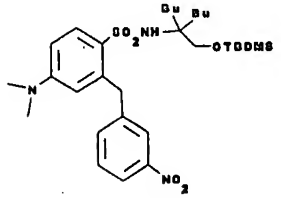


Example 13

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide and (4*S*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide



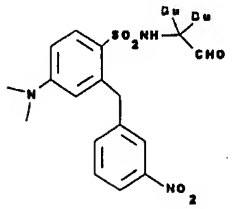
Step 1. *N*-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide



To a solution of 2.0 g (4.25 mmol) of the material prepared in Step 4 of Example 1 above in 10 mL of tetrahydrofuran cooled to 0 °C was added 8.0 mL of 1.6 M *n*-butyllithium in hexane. The reaction mixture was stirred at 0 °C for 30 minutes. To the reaction mixture was added 1.9 mL of trimethyl

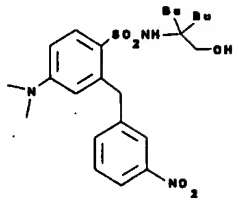
borate and the mixture stirred 10 minutes at 0 °C and then one hour at room temperature. To the reaction mixture was added 100 mL of water and 5% hydrochloric acid to bring the solution to a pH of 6-7 and then the volatiles were evaporated. To the aqueous solution was added 100 mL of ethyl acetate and the solution extracted. The ethyl acetate layer was washed with water (100 mL) and brine (100 mL), dried over magnesium sulfate and concentrated to form a residue. The residue was dissolved in 7 mL of ethanol and degassed with nitrogen. In a separate flask was placed 150 mg of tetrakis(triphenylphosphine)palladium(0), 10 mL of toluene and 918 mg of 3-nitrobenzaldehyde. The ethanol solution was added to the toluene solution followed by 10 mL of 1 M aqueous sodium carbonate. The reaction mixture was heated to reflux for one hour, cooled to room temperature, and then stirred for 16 hours. The reaction mixture was concentrated and dissolved in 100 mL of ethyl acetate. The ethyl acetate solution was washed with water (100 mL) and brine (100 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to form a residue. The residue was purified by flash chromatography to give 1.72 g of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide.

Step 2. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide



The procedure of Step 8 of Example 1 was followed except that *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

Step 3. *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl) methyl]benzenesulfonamide



To a solution of 79 µL of oxalyl chloride in 2 mL of dichloromethane cooled to -78 °C was added 107 µL of dimethylsulfoxide and the mixture stirred 20 minutes. To the cooled reaction mixture was added a solution of 370 mg (0.75 mmol) of the alcohol from Step 2 above in 2 mL of dichloromethane and the mixture was stirred one hour at -78 °C. To the cooled reaction mixture was added 660 µL of diisopropylethylamine. The reaction mixture was warmed to room temperature and stirred for 30 minutes. To the reaction mixture was added 100 mL of water and mixture was extracted with dichloromethane (2 x 50 mL). The combined dichloromethane layers were washed with brine (50 mL), dried over magnesium sulfate and concentrated to give 0.47 g of a yellow oil. The residue was dissolved in 25 mL of 25% ethyl acetate in hexane and filtered through silica and concentrated. The residue was crystallized with ethyl acetate and hexane to

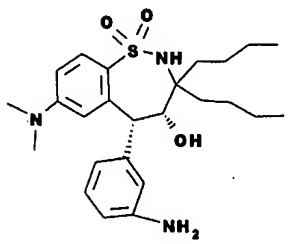
give 301.6 mg of *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide as a yellow solid.

Step 4. (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide and (4*S*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

To a solution of 150 mg (0.31 mmol) of the material prepared in Step 3 above in 6 mL of tetrahydrofuran cooled to -15 °C was added 0.90 mL 1 M of potassium *t*-butoxide in tetrahydrofuran. The reaction mixture was stirred for 15 minutes at -15 °C and then water was added. The organics were evaporated and 100 mL of ethyl acetate was added and then extracted. The ethyl acetate layer was washed with brine (100 mL), dried over magnesium sulfate and concentrated to form a residue. The residue was purified by flash chromatography with 30% ethyl acetate in hexane as eluent to give 61.8 mg of (4*S*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide, and 65.7 mg of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide. ^{1}H NMR and mass spectra were consistent with the product.

Example 14

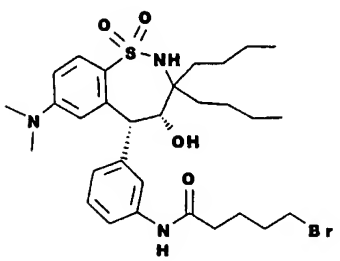
(4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin-4-ol 1,1-dioxide



The procedure of Example 2 above was followed except that (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide. ^{1}H NMR was consistent with the product. MS (M$^+$) 460.

Example 15

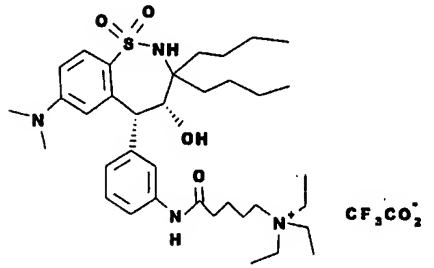
5-bromo-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl)phenyl]pentanamide



The procedure of Example 3 above was followed except that (4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide. ^{1}H NMR was consistent with the product. MS (M+H$^+$) 623.

Example 16

5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-5-oxo-1-pentanaminium trifluoroacetate

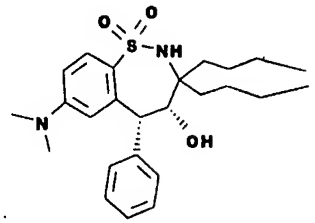


To a solution of 54.1 mg (0.09 mmol) of the bromide prepared in Example 15 above in 1 mL of tetrahydrofuran was added 48 μL of triethylamine. The reaction mixture was heated at reflux for three days. The solvent was evaporated and the residue triturated with ether. The solid was purified by reverse phase high pressure liquid chromatography to give 17.9 mg of 5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-

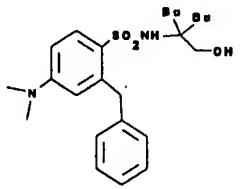
5-oxo-1-pentanaminium trifluoroacetate as a white solid. ^{1}H NMR was consistent with the product. MS (M^+) 643.

Example 17

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2-benzothiazepin-4-ol 1,1-dioxide



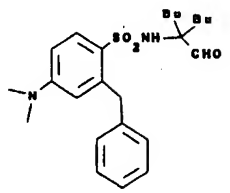
Step 1-2. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-(phenylmethyl)benzenesulfonamide



The procedure of Steps 1-2 of Example 7 was followed except that *N*-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)benzenesulfonamide and benzyl chloride were used in place of *N*-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-*N*-methylbenzenesulfonamide and *p*-methoxybenzyl

chloride.

Step 3. *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-(phenylmethyl) benzenesulfonamide



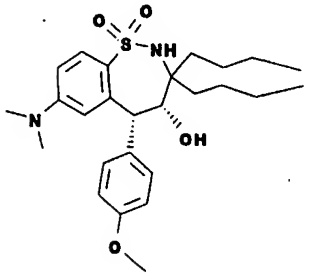
The procedure of Step 3 of Example 13 was followed except that *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-(phenylmethyl) benzenesulfonamide was used in place of *N*-[1-butyl-1-(hydroxymethyl) pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide.

Step 4. (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2-benzothiazepin-4-ol 1,1-dioxide

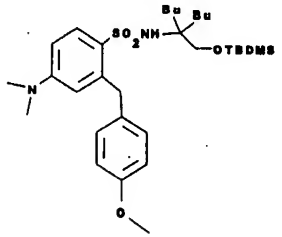
The procedure Step 4 of Example 7 was followed except that *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-(phenylmethyl) benzenesulfonamide was used in place of *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzene-sulfonamide. ^{1}H NMR ($CDCl_3$) δ 0.9 (m, 6H), 1-1.7 (m, 13H), 2.3 (m, 1H), 2.8 (s, 6H), 4.0 (s, 2H), 5.5 (s, 1H), 5.9 (s, 1H), 6.5 (m, 1H), 7.4 (m, 3H), 7.5 (m, 2H), 7.8 (m, 1H). MS ($M+H^+$) 445.0.

Example 18

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

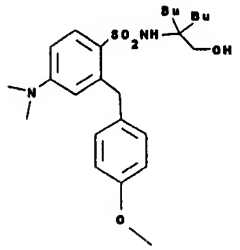


Step 1. *N*-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]benzenesulfonamide



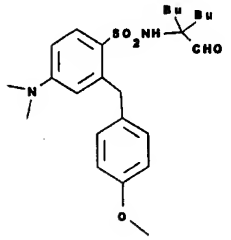
The procedure of Step 1 of Example 7 was followed except that *N*-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-*N*-methylbenzenesulfonamide.

Step 2. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]benzenesulfonamide



The procedure of Step 8 of Example 1 was followed except that *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

Step 3. *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]benzenesulfonamide



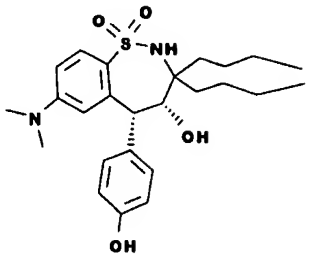
The procedure of Step 3 of Example 13 was followed except that *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl) methyl]benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

Step 4. (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

The procedure of Step 10 of Example 1 was followed except that *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl] benzenesulfonamide was used in place of *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide. ^{1}H NMR ($CDCl_3$) δ 0.89-1.00 (m, 6H), 1.06-1.73 (m, 11H), 2.36 (t, *J* = 9.5 Hz, 1H), 2.80 (s, 6H), 2.98 (s, 1H), 3.85 (s, 3H), 3.97 (s, 1H), 4.03 (d, *J* = 9.0 Hz, 1H), 5.47 (s, 1H), 6.00 (d, *J* = 2.4 Hz, 1H), 6.50 (dd, *J* = 2.6, 8.9 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.81 (d, *J* = 8.7 Hz, 1H).

Example 19

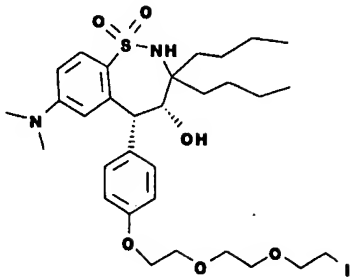
(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide



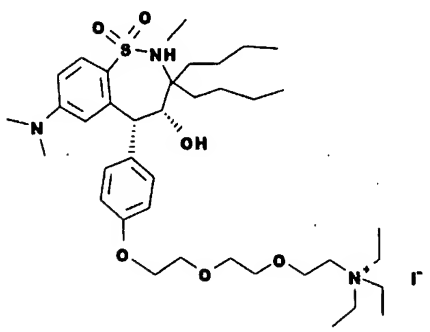
The procedure set forth in Example 8 above was followed except that (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide and a reaction temperature of 0 °C was employed. ^{1}H NMR ($CDCl_3$) δ 0.86-0.97 (m, 6H), 1.15-1.75 (m, 11H), 2.35 (t, *J* = 9.9 Hz, 1H), 2.80 (s, 6H), 3.98 (s, 1H), 4.02 (d, *J* = 8.6 Hz, 1H), 5.12 (s, 1H), 5.45 (s, 1H), 5.98 (d, *J* = 2.4 Hz, 1H), 6.48 (dd, *J* = 2.6, 8.6 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 8.7 Hz, 1H).

Example 20

2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-*N*,*N*,*N*-triethylethanaminium iodide



Step 1



The procedure set forth in Example 9 above was followed except that (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide was used in place of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide and 3.3 equivalents of 95% sodium hydride was used instead of 2.2 equivalents. ^{1}H NMR was consistent with the product.

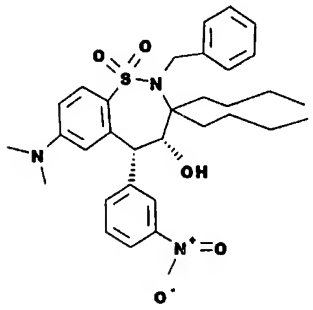
Step 2. 2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-*N*,*N*,*N*-triethylethanaminium iodide

The procedure set forth in Example 10 above was followed except that the benzothiazepine prepared in Step 1 above was used. ^{1}H NMR ($CDCl_3$) δ 0.88-0.05 (m, 6H), 1.14-1.60 (m, 20H), 2.31-2.39 (m, 1H), 2.82 (s, 6H), 3.06-

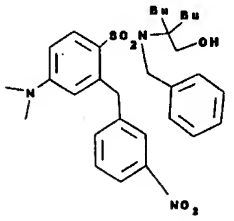
3.15 (m, 2H), 3.54 (q, *J* = 7.3 Hz, 6H), 3.75-3.81 (m, 4H), 3.88-4.17 (m, 7H), 5.47 (s, 1H), 5.98-6.02 (m, 1H), 6.47-6.54 (m, 1H), 6.93-6.98 (m, 2H), 7.42-7.47 (m, 2H), 7.81-7.84 (m, 1H).

Example 21

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

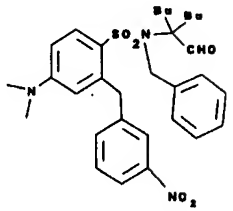


Step 1. *N*-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-(phenylmethyl) benzenesulfonamide



To a solution of 4.24 g (7.0 mmol) of the sulfonamide prepared in Step 1 of Example 13 in 30 mL of acetone was added 2.90 g of potassium carbonate, 0.517 g of tetra-*n*-butylammonium iodide then 2.394 g of benzyl bromide. The reaction mixture was heated at reflux for five days. To the reaction mixture was added 2.394 g of benzyl bromide, 0.517 g of tetra-*n*-butylammonium iodide, and then 2.90 g of powdered potassium carbonate. The reaction mixture was heated at reflux for one day. To the reaction mixture 250 mL of ethyl acetate was added. The ethyl acetate solution was washed with water (3 x 100 mL) and brine (200 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to a residue. The residue was purified by flash chromatography to give 1.82 g of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide.

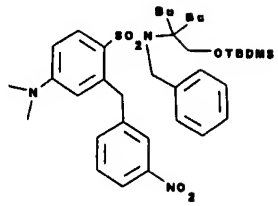
Step 2. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide



The procedure of Step 8 of Example 1 was followed except that *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-(phenylmethyl) benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-

dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

Step 3. *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide



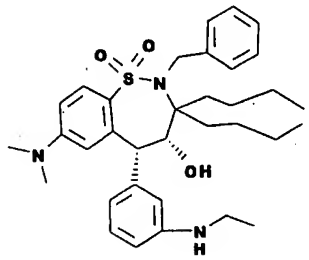
The procedure of Step 3 of Example 13 was followed except that *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl) methyl]-*N*-(phenylmethyl)benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]benzenesulfonamide.

Step 4. (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

The procedure of Step 10 of Example 1 was followed except that *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide was used in place of *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide. ^{1}H NMR was consistent with the product. MS (M+H$^+$) 580.

Example 22

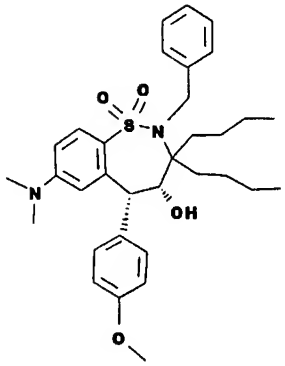
(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5-tetrahydro-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide



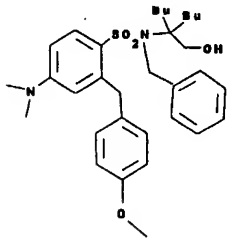
To a solution of 50 mg (0.09 mmol) of the compound prepared in Step 4 of Example 21 in 50 mL ethanol was added about 10 mg of Pearlman's Catalyst. This mixture was hydrogenated at 60 psi H_2 for 20 hours. To the reaction mixture was added about 10 mg of Pearlman's Catalyst and the mixture was hydrogenated at 60 psi at 60 °C for 20 hours. The reaction mixture was filtered and washed with 50 mL of ethyl acetate. The filtrate was washed with water (2 x 50 mL) and brine (50 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 39.8 mg of a residue. The residue was purified by flash chromatography to give 12.6 mg of (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5-tetrahydro-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide. ^{1}H NMR ($CDCl_3$) δ 0.72 (t, *J* = 6.6, 3H), 0.90 (t, *J* = 7.4 Hz), 1.00-1.98 (m, 15H), 2.81 (s, 6H), 3.17 (q, *J* = 7.2 Hz, 2H), 4.15 (d, *J* = 7.8 Hz, 1H), 4.39 (s, 2H), 5.69 (s, 1H), 6.12 (s, 1H), 6.47 (dd, *J* = 2.7, 9.0 Hz, 1H), 6.61-6.65 (m, 1H), 6.78-6.83 (m, 1H), 6.95-7.00 (m, 1H), 7.16-7.31 (m, 5H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.81 (d, *J* = 8.7 Hz, 1H). MS ($M+H^+$) 578.

Example 23

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

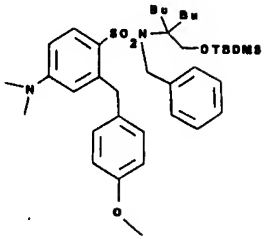


Step 1. *N*-[1-Butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide



To a solution of 2.15 g (4.05 mmol) of the sulfonamide prepared in Step 1 of Example 7 above in 30 mL of dimethylformamide was added 123 mg of 95% sodium hydride and then 964 µL of benzyl bromide. The reaction mixture was stirred 18 hours. To the reaction mixture was added 250 mL of ethyl acetate and the mixture was washed with saturated sodium bicarbonate solution (100 mL) and brine (150 mL). The ethyl acetate layer was dried over magnesium sulfate and concentrated to give 2.88 g of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide.

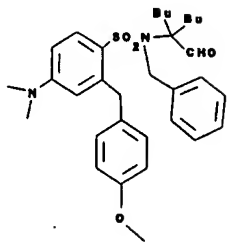
Step 2. *N*-[1-Butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide



The procedure of Step 8 of Example 1 was followed except that *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

Step 3. *N*-[1-Butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-

nitrophenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide



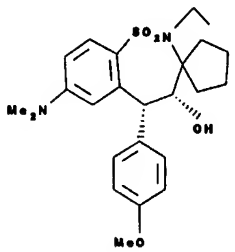
The procedure of Step 3 of Example 13 was followed except that *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide.

Step 4. (4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide

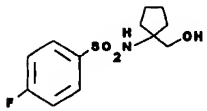
The procedure of Step 10 of Example 1 was followed except that *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-(phenylmethyl)benzenesulfonamide was used in place of *N*-[1-butyl-1-formylpentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide. ^{1}H NMR ($CDCl_3$) δ 0.7 (m, 3H), 0.9 (m, 3H), 1-1.7 (m, 10H), 1.9 (m, 1H), 2.1 (m, 1H), 2.8 (s, 6H), 3.8 (s, 3H), 4.1 (s, 1H), 4.4 (s, 2H), 5.8 (s, 1H), 6.0 (s, 1H), 6.5 (m, 1H), 7.0 (d, J = 8 Hz, 1H), 7.1-7.5 (m, 7H), 7.8 (m, 1H).

Example 24

(4*R*,5*R*)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-spiro[1,2-benzothiazepine-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide

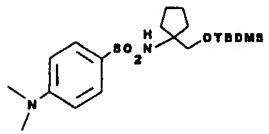


Step 1. *N*-[1-(hydroxymethyl)cyclopentyl]-4-fluorobenzenesulfonamide



The procedure of Step 2 of Example 1 was followed except that cycloleucinol was substituted for 2-amino-2-butylhexanol.

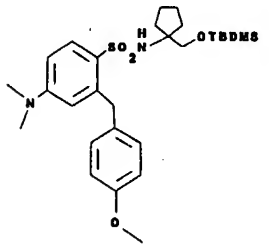
Step 2-3. *N*-[1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]cyclopentyl]-4-(dimethylamino)benzenesulfonamide



The procedure of Steps 3 and 4 of Example 1 was followed except that

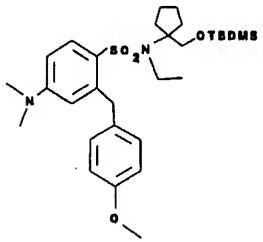
N-[1-(hydroxymethyl)cyclopentyl]-4-fluorobenzenesulfonamide was used in place of *N*-[1-butyl-1-(hydroxymethyl)pentyl]-4-fluorobenzenesulfonamide.

Step 4. *N*-[1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]cyclopentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-methylbenzenesulfonamide



The procedure of Step 1 of Example 7 was followed except that *N*-[1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]cyclopentyl]-4-(dimethylamino)benzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1,1dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-*N*-methylbenzenesulfonamide.

Step 5. *N*-[1-(hydroxymethyl)cyclopentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-ethylbenzenesulfonamide



To a solution of 0.25 g (0.49 mmol) of the sulfonamide prepared in Step 4 above in 5 mL of tetrahydrofuran was added 25 mg of 95% sodium hydride. After 15 minutes, 125 µL of ethyl iodide was added to the reaction mixture. The reaction mixture was stirred 16 hours. To the reaction mixture was added 5 mL of dimethylformamide and the mixture stirred four hours. To the reaction mixture 100 mL of water was added and the mixture extracted with 100 mL of ethyl acetate. The ethyl acetate layer was washed with brine (100 mL), dried over magnesium sulfate and concentrated to give 0.27g of an oil.

Step 6-8. (4*R*,5*R*)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-spiro[1,2-benzothiazepine-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide

The procedure of Steps 8-10 of Example 1 was followed except that *N*-[1-(hydroxymethyl)cyclopentyl]-4-(dimethylamino)-2-[(4-methoxyphenyl)methyl]-*N*-ethylbenzenesulfonamide was used in place of *N*-[1-butyl-1-[[[(1-dimethylethyl)dimethylsilyl]oxy]methyl]pentyl]-4-(dimethylamino)-2-[(3-nitrophenyl)methyl]-*N*-methylbenzenesulfonamide. ^{1}H NMR was consistent with product. MS (M+H$^+$) 445.

Biological Assays

The utility of the compounds of the present invention is shown by the following assays. These assays are performed *in vitro* and in animal models essentially using a procedure recognized to show the utility of the present invention.

In Vitro Assay Of Compounds That Inhibit IBAT-Mediated Uptake Of [^{14}C]-Taurocholate (TC) in H14 Cells

Baby hamster kidney cells (BHK) transfected with the cDNA of

human IBAT (H14 cells) are seeded at 60,000 cells/well in 96 well Top-Count tissue culture plates for assays run within 24 hours of seeding; 30,000 cells/well for assays run within 48 hours; and 10,000 cells/well for assays run within 72 hours.

On the day of assay, the cell monolayer is gently washed once with 100 mL assay buffer (Dulbecco's Modified Eagle's medium with 4.5 g/L glucose + 0.2% (w/v) fatty acid free bovine serum albumin ((FAF)BSA). To each well 50 mL of a two-fold concentrate of test compound in assay buffer is added along with 50 mL of 6 mM [^{14}C]-taurocholate in assay buffer (final concentration of 3 mM [^{14}C]-taurocholate). The cell culture plates are incubated two hours at 37° C prior to gently washing each well twice with 100 mL of 4° C Dulbecco's phosphate-buffered saline (PBS) containing 0.2% (w/v) (FAF)BSA. The wells are then gently washed once with 100 mL of 4° C PBS without (FAF)BSA. To each 200 mL of liquid scintillation counting fluid is added, the plates are heat sealed and shaken for 30 minutes at room temperature prior to measuring the amount of radioactivity in each well on a Packard Top-Count instrument.

In Vitro Assay Of Compounds That Inhibit Uptake Of [^{14}C]-Alanine

The alanine uptake assay is performed in an identical fashion to the taurocholate assay, with the exception that labeled alanine is substituted for the labeled taurocholate.

Data from each of the noted compounds in this assay is as set forth in Table 4 below:

Table 4

COMPOUND (EXAMPLE NUMBER)	HUMAN TC IC_{50} (μM)	ALANINE UPTAKE IC_{50}
1	1.2	
2	0.32	
3	0.69	
4	0.083	>100
5	0.97	
6	0.32	
7	0.57	
8	0.58	
10	0.31	
11	0.20	
12	1.2	
13 (cis)	0.044	
13 (trans)	0.21	
14	0.006	
15	0.022	
16	0.0016	
17	0.035	
18	0.026	
19	0.003	>100
20	0.008	
21		>1.0
22	2.5	
24	13.9	

In Vivo Assay Of Compounds That Inhibit Rat Ileal Uptake Of [^{14}C]-Taurocholate into Bile

(See "Metabolism of 3α,7βdihydroxy-7β-methyl-5β-cholanoic acid and 3α,7β-dihydroxy-7α-methyl-5β-cholanoic acid in hamsters" in Biochimica et Biophysica Acta 833 (1985) 196-202 by Une et al.)

Male wistar rats (200-300 g) are anesthetized with inactin @100 mg/kg. Bile ducts are cannulated with a 10 " length of PE10 tubing. The small intestine is exposed and laid out on a gauze pad. A canulae (1/8" luer lock, tapered female adapter) is inserted at 12 cm from the junction of the small intestine and the cecum. A slit is cut at 4 cm from this same junction (utilizing a 8 cm length of ileum). 20 mL of warm Dulbecco's phosphate buffered saline, pH 6.5 (PBS) is used to flush out the intestine segment. The distal opening is cannulated with a 20 cm length of silicone tubing (0.02" I.D. x 0.037" O.D.). The proximal cannulae is hooked up to a peristaltic pump and the intestine is washed for 20 minutes with warm PBS at 0.25 mL/minute. Temperature of the gut segment is monitored continuously. At the start of the experiment, 2.0 mL of control sample ([^{14}C]-taurocholate @ 0.05 mi/mL with 5 mM cold taurocholate) is loaded into the gut segment with a 3 mL syringe and bile sample collection is begun. Control sample is infused at a rate of 0.25 mL/minute for 21 minutes. Bile samples fractions are collected every three minutes for the first 27 minutes of the procedure. After the 21 minutes of sample infusion, the ileal loop is washed out with 20 mL of warm PBS (using a 30 mL syringe), and then the loop is washed out for 21 minutes with warm PBS at 0.25 mL/minute. A second perfusion is initiated as described above but with the test compound being administered as well (21 minutes administration followed by 21 minutes of wash out) and bile sampled every three minutes for the first 27 minutes. If necessary, a third perfusion is performed as above that typically contains the control sample.

Measurement Of Hepatic Cholesterol Concentration (HEPATIC CHOL)

Liver tissue is weighed and homogenized in chloroform:methanol (2:1). After homogenization and centrifugation the supernatant is separated and dried under nitrogen. The residue is dissolved in isopropanol and the cholesterol content is measured enzymatically, using a combination of cholesterol oxidase and peroxidase, as described by Allain, C. A., *et al.* (1974) *Clin. Chem.* 20, 470.

Measurement Of Hepatic HMG CoA-Reductase Activity (HMG COA)

Hepatic microsomes are prepared by homogenizing liver samples in a phosphate/sucrose buffer, followed by centrifugal separation. The final pelleted material is resuspended in buffer and an aliquot is assayed for HMG CoA reductase activity by incubating for 60 minutes at 37° C in the presence of ^{14}C-HMG-CoA (Dupont-NEN). The reaction is stopped by adding 6N HCl followed by centrifugation. An aliquot of the supernatant is separated, by thin-layer chromatography, and the spot corresponding to the enzyme product is scraped off the plate, extracted and radioactivity is determined by scintillation counting. (Reference: Akerlund, J. and Bjorkhem, I. (1990) *J. Lipid Res.* 31, 2159).

Determination Of Serum Cholesterol (SER.CHOL, HDL-CHOL, TGI and VLDL + LDL)

Total serum cholesterol (SER.CHOL) is measured enzymatically using a commercial kit from Wako Fine Chemicals (Richmond, VA); Cholesterol C11, Catalog No. 276-64909. HDL cholesterol (HDL-CHOL) is assayed using this same kit after precipitation of VLDL and LDL with Sigma Chemical Co. HDL Cholesterol reagent, Catalog No. 352-3 (dextran sulfate method). Total serum triglycerides (blanked) (TGI) are assayed enzymatically with Sigma Chemical Co. GPO-Trinder, Catalog No. 337-B. VLDL and LDL

(VLDL + LDL) cholesterol concentrations are calculated as the difference between total and HDL cholesterol.

Measurement Of Hepatic Cholesterol 7-α Hydroxylase Activity (7α-OHase)

Hepatic microsomes are prepared by homogenizing liver samples in a phosphate/sucrose buffer, followed by centrifugal separation. The final pelleted material is resuspended in buffer and an aliquot is assayed for cholesterol 7-a-hydroxylase activity by incubating for 5 minutes at 37° C in the presence of NADPH. Following extraction into petroleum ether, the organic solvent is evaporated and the residue is dissolved in acetonitrile/ methanol. The enzymatic product is separated by injecting an aliquot of the extract onto a C_{18} reversed phase HPLC column and quantitating the eluted material using UV detection at 240nm. (Reference: Horton, J. D., *et al.* (1994) *J. Clin. Invest.* 93, 2084).

Rat Gavage Assay

Male Wister rats (275-300g) are administered IBAT inhibitors using an oral gavage procedure. Drug or vehicle (0.2% Tween 80 in water) is administered once a day (9:00-10:00 a.m.) for four days at varying dosages in a final volume of 2 mL per kilogram of body weight. Total fecal samples are collected during the final 48 hours of the treatment period and analyzed for bile acid content using an enzymatic assay as described below. Compound efficacy is determined by comparison of the increase in fecal bile acid (FBA) concentration in treated rats to the mean FBA concentration of rats in the vehicle group. Table 5 describes the results of this assay when the compound of Example 4 was tested.

Table 5

COMPOUND (EXAMPLE NUMBER)	DOSE (mg/kg/day)	% INCREASE IN FECAL BILE ACID CONCENTRATION
4	5	217.2
4	0.4	157.8
4	0.04	244.0

Measurement Of Fecal Bile Acid Concentration (FBA)

Total fecal output from individually housed hamsters is collected for 24 or 48 hours, dried under a stream of nitrogen, pulverized and weighed. Approximately 0.1 gram is weighed out and extracted into an organic solvent (butanol/water). Following separation and drying, the residue is dissolved in methanol and the amount of bile acid present is measured enzymatically using the 3α-hydroxysteroid steroid dehydrogenase reaction with bile acids to reduce NAD. (Reference: Mashige, F., *et al.* (1981) *Clin. Chem.* 27, 1352).

[^{3}H]taurocholate Uptake in Rabbit Brush Border Membrane Vesicles (BBMV)

Rabbit Ileal brush border membranes are prepared from frozen ileal mucosa by the calcium precipitation method described by Malathi *et al.* (Reference: (1979) *Biochimica Biophysica Acta,* 554, 259). The method for measuring taurocholate is essentially as described by Kramer *et al.* (Reference: (1992) *Biochimica Biophysica Acta,* 1111, 93) except the assay volume is 200 µL instead of 100 µL. Briefly, at room temperature a 190 µL solution containing 2µM [^{3}H]-taurocholate(0.75 µCi), 20 mM tris, 100 mM NaCl, 100 mM mannitol pH 7.4 is incubated for 5 seconds with 10 µL of brush border membrane vesicles (60-120 µg protein). The incubation is initiated by the addition of the BBMV while vortexing and the reaction is stopped by the

addition of 5 mL of ice cold buffer (20 mM Hepes-tris, 150 mM KCl) followed immediately by filtration through a nylon filter (0.2 µm pore) and an additional 5 mL wash with stop buffer.

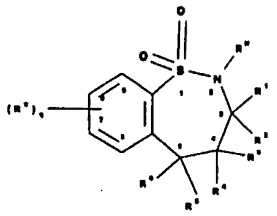
Acyl-CoA: cholesterol Acyl Transferase (ACAT)

Hamster liver and rat intestinal microsomes are prepared from tissue as described previously (Reference: (1980) *J. Biol. Chem.* 255, 9098) and used as a source of ACAT enzyme. The assay consists of a 2.0 mL incubation containing 24 µM Oleoyl-CoA (0.05 µCi) in a 50 mM sodium phosphate, 2 mM DTT ph 7.4 buffer containing 0.25 % BSA and 200 µg of microsomal protein. The assay is initiated by the addition of oleoyl-CoA. The reaction proceeds for five minutes at 37° C and is terminated by the addition of 8.0 mL of chloroform/methanol (2:1). To the extraction is added 125 µg of cholesterol oleate in chloroform methanol to act as a carrier and the organic and aqueous phases of the extraction are separated by centrifugation after thorough vortexing. The chloroform phase is taken to dryness and then spotted on a silica gel 60 TLC plate and developed in hexane/ethyl ether (9:1). The amount of cholesterol ester formed is determined by measuring the amount of radioactivity incorporated into the cholesterol oleate spot on the TLC plate with a Packard instaimager. The examples herein can be repeated with similar success by substituting the generically or specifically described reactants and/or operating conditions of this invention for those used in the preceding examples.

The invention being thus described, it is apparent that the same can be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the present invention, and all such modifications and equivalents as would be obvious to one skilled in the art are intended to be included within the scope of the following claims.

What is claimed is:

1. A compound of formula (I):



wherein:
q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

R^3 and R^4 are independently selected from the group consisting of hydrogen; hydrocarbyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^9 and R^{10} are independently selected from the group consisting of hydrogen; hydrocarbyl; amino; and hydrocarbylamino; wherein said hydrocarbyl moeities may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl moieties optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; hydrocarbyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; wherein said hydrocarbyl moeities may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl moieties optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

R^5 and R^6 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; $-NO_2$; -CN; oxo; hydrocarbyl; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen or hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally

substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein A^- is a pharmaceutically acceptable anion, and M is a pharmaceutically acceptable cation; and

wherein R^9 is as defined above; or

R^4 and R^6 together represent a bond; and

R^N is selected from the group consisting of hydrogen and hydrocarbyl, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus;

one or more R^X radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; hydrocarbyl; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-S(O)_2R^{13}$; $-SO_3R^{13}$; $-S^+R^{13}R^{14}A^-$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-NR^{14}C(O)R^{13}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-S(O)_nNR^{13}R^{14}$; $-N^+R^{13}R^{14}R^{15}A^-$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue, wherein said hydrocarbyl may be optionally substituted with one or more groups comprising one or more heteroatoms, and wherein said hydrocarbyl optionally may have one or more carbon atoms replaced by one or more heteroatoms independently selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus; and

wherein n is 0, 1 or 2; and

wherein R^{13}, R^{14}, R^{15}, A^-, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

provided that at least one of R^1, R^2, R^3, R^4, R^5, and R^6 is a radical other than hydrogen or alkyl; and

provided that when R^5 or R^6 is aryl, the other of R^5 and R^6 is a radical other than heterocycylalkyl.

2. A compound of claim 1 wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl;

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^wA^-$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P(O)R^9$-; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; carboxyalkylamino; alkoxyalkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3 and R^4 are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cyanoalkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

R^5 and R^6 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may have one or more carbons replaced by -O-; $-NR^7-$; $-N^+R^7R^8A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^7A^-$; $-PR^7-$; $-P(O)R^7-$; $-P^+R^7R^8A^-$; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-P^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminoalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^{9}$-; $-N^{+}R^{9}R^{10}A^{-}$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{9}A^{-}$-; $-PR^{9}$-; $-P^{+}R^{9}R^{10}A^{-}$-; $-P(O)R^{9}$-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^{9} and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{w}, and A^{-} are as defined above; and

R^{N} is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aralkyl; and heterocyclylalkyl; and

one or more R^{X} radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-S(O)_2R^{13}$; $-SO_3R^{13}$; $-S^{+}R^{13}R^{14}A^{-}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-NR^{14}C(O)R^{13}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-OR^{18}$; $-S(O)_nNR^{13}R^{14}$; $-NR^{13}R^{18}$; $-NR^{18}OR^{14}$; $-N^{+}R^{13}R^{14}R^{15}A^{-}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue;

wherein the R^{x} alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-P^{9}R^{10}$; $-P^{+}R^{9}R^{11}R^{12}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

wherein the R^{x} quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl;

hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; -C(O)$NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-P^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; $-P(OR^{13})OR^{14}$; $-S^{+}R^{13}R^{14}A^{-}$; $-N^{+}R^{13}R^{14}R^{15}A^{-}$; and carbohydrate residue; and

wherein the R^{X} radicals comprising carbon optionally may have one or more carbons replaced by -O-; $-NR^{13}$-; $-N^{+}R^{13}R^{14}A^{-}$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{13}A^{-}$-; $-PR^{13}$-; $-P(O)R^{13}$-; $-PR^{13}R^{14}$; $-P^{+}R^{13}R^{14}A^{-}$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; $-NR^{9}$-; $-N^{+}R^{9}R^{10}A^{-}$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{9}A^{-}$-; $-PR^{9}$-; $-P^{+}R^{9}R^{10}A^{-}$-; or $-P(O)R^{9}$-; and

wherein R^{18} is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R^{18} alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN ; NO_2; oxo; $-OR^{9}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{11}R^{12}A^{-}$; $-SR^{9}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{9}$; $-CO_2R^{9}$; $-CONR^{9}R^{10}$; $-SO_2OM$; $-SO_2NR^{9}R^{10}$; $-PR^{9}R^{10}$; $-P(OR^{13})OR^{14}$; $-PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{w}, A^{-}, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

3. A compound of claim 1 wherein:

q is an integer from 1 to 4;

R^{1} and R^{2} are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl;

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^WA^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^WA^-$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1 and R^2 alkyl; cycloalkyl; alkenyl; alkynyl; arylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9$-; $-N^+R^9R^{10}A^-$-, -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-, $-PR^9$-; $-P(O)R^9$-; $-P^+R^9R^{10}A^-$-, or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; carboalkoxyalkyl; carboxyheterocyclyl; carboxyalkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3 and R^4 are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; carboxyalkyl; carboalkoxyalkyl; cycloalkyl; cyanoalkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

R^5 and R^6 are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$;- CO_2R^7; $-CONR^7R^8$; $-N^+R^7R^8R^9A$-; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may have one or more carbons replaced by -O-; $-NR^7$-; $-N^+R^7R^8A$-; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$-; $-PR^7$-; $-P(O)R^7$-; $-P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen and alkyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; sulfoalkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^{9}R^{10}$; $-P^{+}R^{9}R^{10}R^{11}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^{9}$-; $-N^{+}R^{9}R^{10}A^{-}$; -S-; -SO-; $-SO_2$-; $-S^{+}R^{9}A^{-}$; $-PR^{9}$-; $-P^{+}R^{9}R^{10}A^{-}$; $-P(O)R^{9}$-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^{9} and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{w}, and A^{-} are as defined above; and

R^{N} is selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; and aralkyl; and

one or more R^{x} radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; alkyl; cycloalkyl; polyalkyl;

haloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; polyether; acyloxy; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-S(O)_2R^{13}$; $-SO_3R^{13}$; $-S^{+}R^{13}R^{14}A^{-}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-NR^{14}C(O)R^{13}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-OR^{18}$; $-S(O)_nNR^{13}R^{14}$; $-NR^{13}R^{18}$; $-NR^{18}OR^{14}$; $-N^{+}R^{13}R^{14}R^{15}A^{-}$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; amino acid residue; peptide acid residue; polypeptide acid residue; and carbohydrate acid residue;

wherein the R^{x} alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; and acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^{9}R^{10}$; $-P^{+}R^{9}R^{11}R^{12}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

wherein the R^{x} quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; $-P(OR^{13})OR^{14}$; $-S^{+}R^{13}R^{14}A^{-}$; and $-N^{+}R^{13}R^{14}R^{15}A^{-}$; and carbohydrate residue; and

wherein the R^{x} radicals comprising carbon optionally may have one or more carbons replaced by -O-; $-NR^{13}$-; $-N^{+}R^{13}R^{14}A^{-}$; -S-; -SO-; $-SO_2$-; $-S^{+}R^{13}A^{-}$; $-PR^{13}$-; -P(O)R^{13}-; $-PR^{13}$-; $-P^{+}R^{13}R^{14}A^{-}$; phenylene; amino acid; peptide; polypeptide; carbohydrate; polyether; or polyalkyl; wherein said phenylene; amino acid; peptide; polypeptide; carbohydrate; and polyalkyl optionally may have one or more carbons replaced by -O-; $-NR^{9}$-; $-N^{+}R^{9}R^{10}A^{-}$; -S-; -SO-; $-SO_2$-; $-S^{+}R^{9}A^{-}$; $-PR^{9}$-; $-P^{+}R^{9}R^{10}A^{-}$; or $-P(O)R^{9}$-; and

wherein R^{18} is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl;

heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R^{18} alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN ; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{11}R^{12}A^-$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; $-CONR^9R^{10}$; $-SO_2OM$; $-SO_2NR^9R^{10}$; $-PR^9R^{10}$; $-P(OR^{13})OR^{14}$; $-PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^w, A^-, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

4. A compound of claim 1 wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkenyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkynyl; (C_1-C_{10})alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form (C_3-C_{10})cycloalkyl;

wherein the R^1 and R^2 (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkenyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkynyl; (C_1-C_{10})alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^wA^-$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1 and R^2 (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkenyl; (C_1-C_{10})alkoxy(C_2-C_{10})alkynyl; (C_1-C_{10})alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$-; $-PR^9$; $-P(O)R^9$-; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3 and R^4 are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; (C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; cyano(C_1-C_{10})alkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

R^5 and R^6 are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; $-OR^9$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$;

wherein the R^5 and R^6 (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; (C_1-C_{10})alkyl; polyalkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$;

$-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the (C_1-C_{10})alkyl, polyalkyl, halo(C_1-C_{10})alkyl, hydroxy(C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, aryl(C_1-C_{10})alkyl, heterocyclyl(C_1-C_{10})alkyl, and polyether substituents of the R^5 and R^6 radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the (C_1-C_{10})alkyl, polyalkyl, halo(C_1-C_{10})alkyl, hydroxy(C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl, (C_2-C_{10})alkenyl, (C_2-C_{10})alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, aryl(C_1-C_{10})alkyl, heterocyclyl(C_1-C_{10})alkyl, and polyether substituents of the R^5 and R^6 radicals optionally may have one or more carbons replaced by -O-; $-NR^7-$; $-N^+R^7R^8A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^7A^-$; $-PR^7-$; $-P(O)R^7-$; $-P^+R^7R^8A^-$; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen and (C_1-C_{10})alkyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaryl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaryl (C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aminocarbonyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkylaminocarbonyl (C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; (C_1-C_{10})alkyl; sulfo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; - $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaryl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aminocarbonyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkylaminocarbonyl(C_1-C_{10})alkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$; $-PR^9-$; $-P^+R^9R^{10}A^-$; $-P(O)R^9-$; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as defined above; and

R^N is selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; and aryl(C_1-C_{10})alkyl; and

one or more R^X radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; halo(C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; polyether;

acyloxy; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -$S(O)R^{13}$; -$S(O)_2R^{13}$; -SO_3R^{13}; -$S^+R^{13}R^{14}A^-$; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$NR^{14}C(O)R^{13}$; -$C(O)NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -OR^{18}; -$S(O)_nNR^{13}R^{14}$; -$NR^{13}R^{18}$; -$NR^{18}OR^{14}$; -$N^+R^{13}R^{14}R^{15}A^-$; -$PR^{13}R^{14}$; -$P(O)R^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide acid residue; polypeptide acid residue; and carbohydrate acid residue;

wherein the R^x (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; halo(C_1-C_{10})alkyl; hydroxy(C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; and acyloxy radicals optionally may be further substituted with halogen; -CN; oxo; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{11}R^{12}A^-$; -SR^{16}; -$S(O)R^9$; -SO_2R^9; -SO_3R^{16}; -CO_2R^{16}; -$CONR^9R^{10}$; -$SO_2NR^9R^{10}$; -$PO(OR^{16})OR^{17}$; -PR^9R^{10}; -$P^+R^9R^{11}R^{12}A^-$; or -$S^+R^9R^{10}A^-$; and

wherein the R^x quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; -NO_2; oxo; (C_1-C_{10})alkyl; (C_3-C_{10})cycloalkyl; polyalkyl; halo(C_1-C_{10})alkyl; hydroxy(C_1-C_{10})alkyl; (C_2-C_{10})alkenyl; (C_2-C_{10})alkynyl; aryl; heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -$S(O)R^{13}$; -SO_2R^{13}; -SO_3R^{13}; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$C(O)NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -$P(O)R^{13}R^{14}$; -$PR^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; -$P(OR^{13})OR^{14}$; -$S^+R^{13}R^{14}A^-$; and -$N^+R^{13}R^{14}R^{15}A^-$; and

wherein the R^x radicals comprising carbon optionally may have one or more carbons replaced by -O-; -NR^{13}-; -$N^+R^{13}R^{14}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^{13}A^-$-; -PR^{13}-; -$P(O)R^{13}$-; -PR^{13}-; -$P^+R^{13}R^{14}A^-$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; -NR^9-; -$N^+R^9R^{10}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^9A^-$-; -PR^9-; -$P^+R^9R^{10}A^-$-; or -$P(O)R^9$-; and

wherein R^{18} is selected from the group consisting of (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; acyl; and aryl(C_1-C_{10})alkoxycarbonyl; and

wherein the R^{18} (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; acyl; and aryl(C_1-C_{10})alkoxycarbonyl radicals optionally

may be substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; -OR^9; -NR^9R^{10}; -$N^+R^9R^{11}R^{12}A^-$; -SR^9; -$S(O)R^9$; -SO_2R^9; -SO_3R^9; -CO_2R^9; -$CONR^9R^{10}$; -SO_2OM; -$SO_2NR^9R^{10}$; -PR^9R^{10}; -$P(OR^{13})OR^{14}$; -$PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^x, A^-, and M are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

provided that aryl is selected from the group consisting of optionally substituted phenyl, biphenyl and naphthyl; and

provided that heterocyclyl is selected from the group consisting of optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.

5. A compound of claim 1 wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, hexyl, phenoxymethylene, phenoxyethylene, phenoxypropylene, pyridinyloxymethylene, pyridinyloxyethylene; methylpyridinyloxymethylene, methylpyridinyloxyethylene, pyrimidinyloxymethylene, and pyrimidinyloxyethylene; or

R^1 and R^2 taken together with the carbon to which they are attached form cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl; and

R^3 and R^4 are independently selected from the group consisting of hydrogen, hydroxy, methyl, ethyl, phenyl, pyridinyl, amino, methylamino, dimethylamino, ethylamino and diethylamino; and

R^5 and R^6 are independently selected from the group consisting of hydrogen, phenyl, chlorophenyl, fluorophenyl, bromophenyl, iodophenyl, hydroxyphenyl, methoxyphenyl, ethoxyphenyl, methoxy(chlorophenyl), methoxy(fluorophenyl), methoxy(bromophenyl), methoxy(iodophenyl), ethoxy(chlorophenyl), ethoxy(fluorophenyl), ethoxy(bromophenyl), ethoxy(iodophenyl), nitrophenyl, aminophenyl, methylaminophenyl, dimethylaminophenyl, ethylaminophenyl, diethylaminophenyl, trimethylammoniumphenyl, triethylammoniumphenyl,

trimethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl, triethylammoniumethylcarbonylaminophenyl, trimethylammoniumpropylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl, trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl, chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, ethylcarbonylaminophenyl, chloroethylcarbonylaminophenyl, fluoroethylcarbonylaminophenyl, bromoethylcarbonylaminophenyl, iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl, chloropropylcarbonylaminophenyl, fluoropropylcarbonylaminophenyl, bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, butylcarbonylaminophenyl, chlorobutylcarbonylaminophenyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl, iodobutylcarbonylaminophenyl, 3,4-dioxymethylenephenyl, pyridinyl, methylpyridinyl, pyridinium, methylpyridinium, thienyl, chlorothienyl, fluorothienyl, bromothienyl, iodothienyl; methoxycarbonylphenyl, ethoxycarbonylphenyl, trimethylammoniumethoxyethoxyethoxyphenyl, triethylammoniumethoxyethoxyethoxyphenyl, chloroethoxyethoxyethoxyphenyl, fluoroethoxyethoxyethoxyphenyl, bromoethoxyethoxyethoxyphenyl, iodoethoxyethoxyethoxyphenyl, pyridiniumethoxyethoxyethoxyphenyl, piperazinyloxymethoxyethoxyethoxyphenyl, methylpiperazinyloxymethoxyethoxyethoxyphenyl, dimethylpiperazinyloxymethoxyethoxyethoxyphenyl, piperidinyloxymethoxyethoxyethoxyphenyl, methylpiperidinyloxymethoxyethoxyethoxyphenyl, and dimethylpiperidinyloxymethoxyethoxyethoxyphenyl; and

R^N is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl and benzyl; and

one or more R^X radicals are independently selected from the group consisting of hydroxy, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl,

tert-butyl, sec-butyl, methoxy, ethoxy, n-propoxy, isopropoxy, methylthio, methylsulfinyl, methylsulfonyl, ethylthio, ethylsulfinyl, ethylsulfonyl, amino, hydroxyamino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, N-methyl-N-carboxymethyl-amino, N,N-dimethyl-N-carboxymethyl-ammonium, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino, n-propylcarbonylamino, n-butylcarbonylamino, n-pentylcarbonylamino, n-hexylcarbonylamino, benzyloxycarbonylamino, aminoimidocarbonylamino, morpholinyl, N-methyl-morpholinium, azetidinyl, N-methyl-azetidinium, pyrrolidine, N-methyl-pyrrolidinium, piperazinyl, N-methylpiperazinyl, N,N'-dimethyl-piperazinium, piperidinyl, methylpiperidinyl, N-methyl-piperidinium, and thienyl; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

6. A compound of claim 1 wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of hydrogen and (C_1-C_{10})alkyl; or

R^1 and R^2 taken together with the carbon to which they are attached form (C_3-C_{10})cycloalkyl; and

R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy; and

R^5 is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from the group consisting of halogen; hydroxy; $-NO_2$; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl$(C_1-$

C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; and $-CONR^9R^{10}$; and

wherein R^9 and R^{10} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^w and R^{16} are as defined in claim 2; and

R^6 is hydrogen; and

R^N is selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; and aryl(C_1-C_{10})alkyl; and

one or more R^X radicals are independently selected from the group consisting of hydrogen; $-NO_2$; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; $-OR^{13}$; $-NR^{13}R^{14}$;

wherein R^{13} and R^{14} are as defined above; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof; and

provided that aryl is selected from the group consisting of optionally substituted phenyl, biphenyl and naphthyl; and

provided that heterocyclyl is selected from the group consisting of optionally substituted heterocyclyl comprising a 5 to 10 membered ring and comprising one or more ring atoms that are heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur and phosphorus.

7. A compound of claim 1 wherein:

q is an integer from 1 to 4;

R^1 and R^2 are independently selected from the group consisting of ethyl and n-butyl; or

R^1 and R^2 taken together with the carbon to which they are attached form cyclopentyl; and

one of R^3 and R^4 is hydrogen and the other of R^3 and R^4 is hydroxy; and

R^5 is selected from the group consisting of phenyl, hydroxyphenyl, methoxyphenyl, ethoxyphenyl, nitrophenyl, aminophenyl, methylaminophenyl, dimethylaminophenyl, ethylaminophenyl, diethylaminophenyl, trimethylammoniumphenyl, triethylammoniumphenyl, trimethylammoniummethylcarbonylaminophenyl, triethylammoniummethylcarbonylaminophenyl, trimethylammoniumethylcarbonylaminophenyl, triethylammoniumethylcarbonylaminophenyl, trimethylammoniumpropylcarbonylaminophenyl, triethylammoniumpropylcarbonylaminophenyl, trimethylammoniumbutylcarbonylaminophenyl, triethylammoniumbutylcarbonylaminophenyl, methylcarbonylaminophenyl, chloromethylcarbonylaminophenyl, fluoromethylcarbonylaminophenyl, bromomethylcarbonylaminophenyl, iodomethylcarbonylaminophenyl, ethylcarbonylaminophenyl, chloroethylcarbonylaminophenyl, fluoroethylcarbonylaminophenyl, bromoethylcarbonylaminophenyl, iodoethylcarbonylaminophenyl, propylcarbonylaminophenyl, chloropropylcarbonylaminophenyl, fluoropropylcarbonylaminophenyl, bromopropylcarbonylaminophenyl, iodopropylcarbonylaminophenyl, butylcarbonylaminophenyl, chlorobutylcarbonylaminophenyl, fluorobutylcarbonylaminophenyl, bromobutylcarbonylaminophenyl, iodobutylcarbonylaminophenyl, trimethylammoniumethoxyethoxyethoxyphenyl, triethylammoniumethoxyethoxyethoxyphenyl, chloroethoxyethoxyethoxyphenyl, fluoroethoxyethoxyethoxyphenyl, bromoethoxyethoxyethoxyphenyl, iodoethoxyethoxyethoxyphenyl, and pyridiniumethoxyethoxyethoxyphenyl; and

R^6 is hydrogen;

R^N is selected from the group consisting of hydrogen, methyl, ethyl, and benzyl; and

one or more R^X radicals are independently selected from the group consisting of hydroxy, methyl, ethyl, methoxy, ethoxy, amino, hydroxyamino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, N-methyl-N-carboxymethyl-amino, N,N-dimethyl-N-carboxymethyl-ammonium, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino, benzyloxycarbonylamino, and aminoimidocarbonylamino; or.

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

8. A compound of claim 1 selected from the compounds of the group consisting of:

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

5-chloro-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]pentanamide;

5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-5-oxo-pentanaminium trifluoroacetate;

2-chloro-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]acetamide;

2-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino]-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-2-oxoethanaminium chloride;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-(((2-iodoethyoxy)ethoxy)ethoxy)phenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

1-[2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]ethyl]pyridinium;

2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-2-methyl-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-*N,N,N*-triethylethanaminium iodide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-methoxyphenyl)-2-methyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide and (4*S*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-5-(3-aminophenyl)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-1,2-benzothiazepin-4-ol 1,1-dioxide;

5-bromo-*N*-[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl)phenyl]pentanamide;

5-[[3-[(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenyl]amino]-*N,N,N*-triethyl-5-oxo-1-pentanaminium trifluoroacetate;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-phenyl-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-hydroxyphenyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

2-[2-[2-[4-[(4*R*,5*R*)-3,3-dibutyl-7- (dimethylamino)-2,3,4,5-tetrahydro-4-hydroxy-1,1-dioxido-1,2-benzothiazepin-5-yl]phenoxy]ethoxy]ethoxy]-*N,N,N*-triethylethanaminium iodide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(3-nitrophenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-5-[3-(ethylamino)phenyl]-2,3,4,5-tetrahydro-2- (phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide;

(4*R*,5*R*)-3,3-dibutyl-7-(dimethylamino)-2,3,4,5-tetrahydro-5-(4-methoxyphenyl)-2-(phenylmethyl)-1,2-benzothiazepin-4-ol 1,1-dioxide; and

(4*R*,5*R*)-7-dimethylamino)-2-ethyl-4,5-dihydro-5-(4-methoxyphenyl)-spiro[1,2-benzothiazepine-3(2H),1'-cyclopentan]-4-ol 1,1-dioxide; and

their pharmaceutically acceptable salts.

9. A compound of claim 2 wherein R^5 and R^6 are independently selected from the group consisting of H; aryl; heterocyclyl; and quaternary heterocyclyl;

wherein the R^5 and R^6 aryl; heterocyclyl; and quaternary heterocyclyl radicals optionally may be substituted with one or more radicals independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -$S(O)R^{13}$; -SO_2R^{13}; -SO_3R^{13}; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$C(O)NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -$NR^{13}C(O)R^{14}$; -$NR^{13}C(O)NR^{14}R^{15}$; -$NR^{13}CO_2R^{14}$; -$OC(O)R^{13}$; -$OC(O)NR^{13}R^{14}$; -$NR^{13}SOR^{14}$; -$NR^{13}SO_2R^{14}$; -$NR^{13}SONR^{14}R^{15}$; -$NR^{13}SO_2NR^{14}R^{15}$; -$PR^{13}R^{14}$; -$P(O)R^{13}R^{14}$; -$PR^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; -$P(OR^{13})OR^{14}$; -$S^+R^{13}R^{14}A^-$; and -$N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; -OR^7; -NR^7R^8; -SR^7; -$S(O)R^7$; -SO_2R^7; -SO_3R^7; -CO_2R^7; -$CONR^7R^8$; -$N^+R^7R^8R^9A^-$; -$P(O)R^7R^8$; -PR^7R^8; -$P^+R^7R^8R^9A^-$; and -$P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^5 and R^6 radicals optionally may have one or more carbons replaced by -O-; -NR^7-; -$N^+R^7R^8A^-$-; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -PR^7-; -$P(O)R^7$-; -$P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^{9}R^{10}$; $-P^{+}R^{9}R^{10}R^{11}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^{9}-$; $-N^{+}R^{9}R^{10}A^{-}-$; -S-; -SO-; $-SO_2-$; $-S^{+}R^{9}A^{-}-$; $-PR^{9}-$; $-P^{+}R^{9}R^{10}A^{-}-$; $-P(O)R^{9}-$; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^{9} and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{w}, and A^{-} are as defined in claim 2.

10. A compound of claim 2 wherein R^{5} or R^{6} has the formula

$$-Ar-(R^{y})_t$$

wherein:

t is an integer from 0 to 5;

Ar is selected from the group consisting of phenyl; thiophenyl; pyridyl; piperazinyl; piperonyl; pyrrolyl; naphthyl; furanyl; anthracenyl; quinolinyl; isoquinolinyl; quinoxalinyl; imidazolyl; pyrazolyl; oxazolyl; isoxazolyl;

pyrimidinyl; thiazolyl; triazolyl; isothiazolyl; indolyl; benzoimidazolyl; benzoxazolyl; benzothiazolyl; and benzoisothiazolyl; and

one or more R^{y} are independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^{+}R^{13}R^{14}R^{15}A^{-}$; $-P(OR^{13})OR^{14}$; $-S^{+}R^{13}R^{14}A^{-}$; and $-N^{+}R^{13}R^{14}R^{15}A^{-}$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^{y} radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^{7}$; $-NR^{7}R^{8}$; $-SR^{7}$; $-S(O)R^{7}$; $-SO_2R^{7}$; $-SO_3R^{7}$; $-CO_2R^{7}$; $-CONR^{7}R^{8}$; $-N^{+}R^{7}R^{8}R^{9}A^{-}$; $-P(O)R^{7}R^{8}$; $-PR^{7}R^{8}$; $-P^{+}R^{7}R^{8}R^{9}A^{-}$; and $-P(O)(OR^{7})OR^{8}$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^{y} radicals optionally may have one or more carbons replaced by -O-; $-NR^{7}-$; $-N^{+}R^{7}R^{8}A^{-}-$; -S-; -SO-; $-SO_2-$; $-S^{+}R^{7}A^{-}-$; $-PR^{7}-$; $-P(O)R^{7}-$; $-P^{+}R^{7}R^{8}A^{-}-$; or phenylene; and

wherein R^{7} and R^{8} are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^{9}R^{10}$; $-N^{+}R^{9}R^{10}R^{w}A^{-}$; $-SR^{16}$; $-S(O)R^{9}$; $-SO_2R^{9}$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^{9}R^{10}$; $-SO_2NR^{9}R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^{9}R^{10}$; $-P^{+}R^{9}R^{10}R^{11}A^{-}$; $-S^{+}R^{9}R^{10}A^{-}$; and carbohydrate residue; and

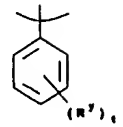
wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^{9}$-; $-N^{+}R^{9}R^{10}A^{-}$-; -S-; -SO-; $-SO_2$-; $-S^{+}R^{9}A^{-}$-; $-PR^{9}$-; $-P^{+}R^{9}R^{10}A^{-}$-; $-P(O)R^{9}$-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^{9} and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^{9}, R^{10}, R^{11}, R^{12}, R^{w}, and A^{-} are as defined in claim 2.

11. A compound of claim 2 wherein at least one of R^{5} and R^{6} has the formula



(II)

wherein R^{y} and t are defined as in claim 10.

12. A compound of claim 11 wherein R^{N} is selected from the group consisting of hydrogen, alkyl and aralkyl.

13. A compound of claim 11 wherein R^{N} is selected from the group consisting of hydrogen, $(C_1\text{-}C_{10})$alkyl and aryl$(C_1\text{-}C_{10})$alkyl.

14. A compound of claim 11 wherein R^{N} is selected from the group consisting of hydrogen, methyl, ethyl and benzyl.

15. A compound of claim 11 wherein R^{1} and R^{2} are independently selected from the group consisting of hydrogen, alkyl, and $(C_3\text{-}C_{10})$cycloalkyl.

16. A compound of claim 11 wherein R^{1} and R^{2} are independently selected from the group consisting of hydrogen and $(C_1\text{-}C_{10})$alkyl.

17. A compound of claim 11 wherein R^{1} and R^{2} are independently selected from the group consisting of $(C_1\text{-}C_{10})$alkyl.

18. A compound of claim 11 wherein R^{1} and R^{2} are independently selected from the group consisting of $(C_1\text{-}C_{7})$alkyl.

19. A compound of claim 11 wherein R^{1} and R^{2} are independently selected from the group consisting of $(C_1\text{-}C_{4})$alkyl.

20. A compound of claim 11 wherein R^1 and R^2 are the same (C_1-C_{10})alkyl.

21. A compound of claim 11 wherein R^1 and R^2 are independently selected from the group consisting ethyl; n-propyl; n-butyl; and isobutyl.

22. A compound of claim 11 wherein R^1 and R^2 are each n-butyl.

23. A compound of claim 11 wherein one of R^1 and R^2 is ethyl and the other of R^1 and R^2 is n-butyl.

24. A compound of claim 11 wherein q is 1, 2, or 3.

25. A compound of claim 11 wherein q is 1 or 2.

26. A compound of claim 11 wherein q is 1.

27. A compound of claim 11 wherein R^3 and R^4 are independently selected from the group consisting of hydrogen and -OR^9.

28. A compound of claim 27 wherein R^9 is hydrogen.

29. A compound of claim 28 wherein said hydroxy group is in a *syn* relationship to said structure of formula (II).

30. A compound of claim 11 wherein R^X radicals are present at the 7-, 8- and 9-positions of the benzo ring of the structure of formula (I).

31. A compound of claim 11 wherein an R^X radical is present at one or more of the 7-, 8-, or 9-positions of the benzo ring of the structure of formula (I).

32. A compound of claim 11 wherein R^X radicals are present at the 7- and 9-positions of the benzo ring of the structure of formula (I).

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33. A compound of claim 11 wherein an R^X radical is present at the 7-position of the benzo ring of the structure of formula (I).

34. A compound of claim 32 wherein said one or more R^X are independently selected from the group consisting of alkyl; aryl; cycloalkyl; heterocyclyl; polyalkyl; acyloxy; polyether; halogen; -OR^{13}; -$NR^{13}R^{14}$; -$NR^{13}NR^{14}R^{15}$; -$N^+R^9R^{11}R^{12}A^-$; -SR^{13}; -$S^+R^{13}R^{14}A^-$; -CO_2R^{13}; and -$NR^{14}C(O)R^{13}$;

wherein alkyl; aryl; cycloalkyl; heterocyclyl; polyalkyl; acyloxy; and polyether; can be further substituted with -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^wA^-$; -SR^{16}; -$S(O)R^9$; -SO_2R^9; -SO_3R^{16}; oxo; -CO_2R^{16}; -CN; halogen; -$CONR^9R^{10}$; -$SO_2NR^9R^{10}$; -$PO(OR^{16})OR^{17}$; -PR^9R^{10}; -$P^+R^9R^{11}R^{12}A^-$; or -$S^+R^9R^{10}A^-$; and

wherein in R^X, one or more carbons are optionally replaced by -O-; -NR^{13}-; -$N^+R^{13}R^{14}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^{13}A^-$-; -PR^{13}-; -$P(O)R^{13}$-; -$P^+R^{13}R^{14}A^-$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; and

wherein in said polyalkyl; phenylene; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue; one or more carbons are optionally replaced by -O-; -NR^9-; -$N^+R^9R^{10}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^9A^-$-; -PR^9-; -$P^+R^9R^{10}A^-$-; or -$P(O)R^9$-.

35. A compound of claim 33 wherein said one or more R^X are independently selected from the group consisting of alkyl; aryl; cycloalkyl; heterocyclyl; polyalkyl; acyloxy; polyether; halogen; -OR^{13}; -$NR^{13}R^{14}$; -$NR^{13}NR^{14}R^{15}$; -$N^+R^9R^{11}R^{12}A^-$; -SR^{13}; -$S^+R^{13}R^{14}A^-$; -CO_2R^{13}; and -$NR^{14}C(O)R^{13}$;

wherein alkyl; aryl; cycloalkyl; heterocyclyl; polyalkyl; acyloxy; and polyether; can be further substituted with -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^wA^-$; -SR^{16}; -$S(O)R^9$; -SO_2R^9; -SO_3R^{16}; oxo; -CO_2R^{16}; -CN; halogen; -$CONR^9R^{10}$; -$SO_2NR^9R^{10}$; -$PO(OR^{16})OR^{17}$; -PR^9R^{10}; -$P^+R^9R^{11}R^{12}A^-$; or -$S^+R^9R^{10}A^-$; and

wherein in R^X, one or more carbons are optionally replaced by -O-; -NR^{13}-; -$N^+R^{13}R^{14}A^-$-; -S-; -SO-; -SO_2-; -$S^+R^{13}A^-$-; -PR^{13}-; -$P(O)R^{13}$-; -

$P^+R^{13}R^{14}A^-$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; and

wherein in said polyalkyl; phenylene; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue; one or more carbons are optionally replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P^+R^9R^{10}A^-$-; or $-P(O)R^9$-.

36. A compound of claim 34 wherein said one or more R^x are independently selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$.

37. A compound of the claim 35 wherein said R^x is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$.

38. A compound of claim 36 wherein said one or more R^x are independently selected from the group consisting of $-OR^{13}$ and $-NR^{13}R^{14}$.

39. A compound of claim 37 wherein said R^x is independently selected from the group consisting of $-OR^{13}$ and $-NR^{13}R^{14}$.

40. A compound of claim 38 wherein R^{13} and R^{14} are each methyl.

41. A compound of the claim 39 wherein R^{13} and R^{14} are each methyl.

42. A compound of claim 11 wherein an R^y substituent is attached at the 3- or the 4-position of the phenyl ring of the structure of formula (II).

43. A compound of claim 11 wherein t is 1 or 2.

44. A compound of claim 42 wherein t is 1 or 2.

45. A compound of claim 11 wherein said one or more R^y are independently selected from the group consisting of hydrogen; halogen; hydroxy; $-NO_2$; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl;

heterocyclyl(C_1-C_{10})alkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; and $-CONR^9R^{10}$; and

wherein R^9, R^{10}, and R^w are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation.

46. A compound of claim 11 wherein said R^y is independently selected from the group consisting of hydrogen, chloro, fluoro, bromo, iodo, hydroxy, methoxy, ethoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, trimethylammoniummethylcarbonylamino,

triethylammoniummethylcarbonylamino,
trimethylammoniumethylcarbonylamino,
triethylammoniumethylcarbonylamino,
trimethylammoniumpropylcarbonylamino,
triethylammoniumpropylcarbonylamino,
trimethylammoniumbutylcarbonylamino,
triethylammoniumbutylcarbonylamino, methylcarbonylamino,
chloromethylcarbonylamino, fluoromethylcarbonylamino,
bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino,
chloroethylcarbonylamino, fluoroethylcarbonylamino,
bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino,
chloropropylcarbonylamino, fluoropropylcarbonylamino,
bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino,
chlorobutylcarbonylamino, fluorobutylcarbonylamino,
bromobutylcarbonylamino, iodobutylcarbonylamino, methoxycarbonyl,
ethoxycarbonyl, trimethylammoniumethoxyethoxyethoxy,
triethylammoniumethoxyethoxyethoxy, chloroethoxyethoxyethoxy,
fluoroethoxyethoxyethoxy, bromoethoxyethoxyethoxy,
iodoethoxyethoxyethoxy, pyridiniumethoxyethoxyethoxy,
piperazinyloxymethoxyethoxyethoxy,
methylpiperazinyloxymethoxyethoxyethoxy,
dimethylpiperazinyloxymethoxyethoxyethoxy,
piperidinyloxymethoxyethoxyethoxy,
methylpiperidinyloxymethoxyethoxyethoxy, and
dimethylpiperidinyloxymethoxyethoxyethoxyphenyl.

47. A compound of claim 11 wherein said one or more R^y are independently selected from the group consisting of hydroxy, methoxy, ethoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, trimethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, trimethylammoniumethylcarbonylamino, triethylammoniumethylcarbonylamino, trimethylammoniumpropylcarbonylamino,

triethylammoniumpropylcarbonylamino,
trimethylammoniumbutylcarbonylamino,
triethylammoniumbutylcarbonylamino, methylcarbonylamino,
chloromethylcarbonylamino, fluoromethylcarbonylamino,
bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino,
chloroethylcarbonylamino, fluoroethylcarbonylamino,
bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino,
chloropropylcarbonylamino, fluoropropylcarbonylamino,
bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino,
chlorobutylcarbonylamino, fluorobutylcarbonylamino,
bromobutylcarbonylamino, iodobutylcarbonylamino,
trimethylammoniumethoxyethoxyethoxy,
triethylammoniumethoxyethoxyethoxy, chloroethoxyethoxyethoxy,
fluoroethoxyethoxyethoxy, bromoethoxyethoxyethoxy,
iodoethoxyethoxyethoxy, and pyridiniumethoxyethoxyethoxy.

48. A compound of claim 11 wherein said one or more R^y are independently selected from the group consisting of trimethylammonium, triethylammonium, trimethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, trimethylammoniumethylcarbonylamino, triethylammoniumethylcarbonylamino, trimethylammoniumpropylcarbonylamino, triethylammoniumpropylcarbonylamino, trimethylammoniumbutylcarbonylamino, triethylammoniumbutylcarbonylamino, trimethylammoniumethoxyethoxyethoxy, and triethylammoniumethoxyethoxyethoxy.

49. A compound of claim 11 wherein:

R^N is selected from the group consisting of hydrogen, alkyl and aralkyl; and

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, and $(C_3\text{-}C_{10})$cycloalkyl.

50. A compound of claim 11 wherein:

R^N is selected from the group consisting of hydrogen, alkyl and aralkyl; and

R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy.

51. A compound of claim 50 wherein said hydroxy group is in a *syn* relationship to said structure of formula (II).

52. A compound of claim 11 wherein:

R^N is selected from the group consisting of hydrogen, alkyl and aralkyl; and

R^X is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^9, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim 2.

53. A compound of claim 11 wherein:

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, and $(C_3\text{-}C_{10})$cycloalkyl; and R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy.

54. A compound of claim 11 wherein:

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, and $(C_3\text{-}C_{10})$cycloalkyl; and R^X is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^9, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim 2.

55. A compound of claim 11 wherein:

R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy; and

R^X is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^9, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim 2.

56. A compound of claim 11 wherein:

R^N is selected from the group consisting of hydrogen, alkyl and aralkyl;

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, and $(C_3\text{-}C_{10})$cycloalkyl; and R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy.

57. A compound of claim 11 wherein:

R^N is selected from the group consisting of hydrogen, alkyl and aralkyl;

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, and $(C_3\text{-}C_{10})$cycloalkyl; and R^X is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^9, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim 2.

58. A compound of claim 11 wherein:

R^N is selected from the group consisting of hydrogen, alkyl and aralkyl;

R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy; and

R^X is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^9, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim 2.

59. A compound of claim 11 wherein:

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, and $(C_3\text{-}C_{10})$cycloalkyl;

R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy; and

R^X is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^9, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim 2.

60. A compound of claim 11 wherein:

R^N is selected from the group consisting of hydrogen, alkyl and aralkyl;

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, and $(C_3$-$C_{10})$cycloalkyl; R^3 and R^4 are independently selected from the group consisting of hydrogen and hydroxy; and

R^X is selected from the group consisting of polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^9, R^{11}, R^{12}, R^{13} and R^{14} are as defined in claim 2.

61. A compound of claim 60 wherein R^N is selected from the group consisting of hydrogen, $(C_1$-$C_{10})$alkyl and aryl$(C_1$-$C_{10})$alkyl.

62. A compound of claim 60 wherein R^N is selected from the group consisting of hydrogen, methyl, ethyl and benzyl.

63. A compound of claim 60 wherein R^1 and R^2 are independently selected from the group consisting of hydrogen and $(C_1$-$C_{10})$alkyl.

64. A compound of claim 60 wherein R^1 and R^2 are independently selected from the group consisting of $(C_1$-$C_{10})$alkyl.

65. A compound of claim 60 wherein R^1 and R^2 are independently selected from the group consisting of $(C_2$-$C_4)$alkyl.

66. A compound of claim 60 wherein R^1 and R^2 are independently selected from the group consisting ethyl; n-propyl; n-butyl; and isobutyl.

67. A compound of claim 60 wherein R^1 and R^2 are each n-butyl.

68. A compound of claim 60 wherein one of R^1 and R^2 is ethyl and the other of R^1 and R^2 is n-butyl.

69. A compound of claim 60 wherein q is 1, 2, or 3.

70. A compound of claim 60 wherein q is 1 or 2.

71. A compound of claim 60 wherein q is 1.

72. A compound of claim 60 wherein R^X radicals are present at the 7-, 8- and 9-positions of the benzo ring of the structure of formula (I).

73. A compound of claim 60 wherein an R^X radical is present at one or more of the 7-, 8-, or 9-positions of the benzo ring of the structure of formula (I).

74. A compound of claim 60 wherein R^X radicals are present at the 7- and 9-positions of the benzo ring of the structure of formula (I).

75. A compound of claim 60 wherein an R^X radical is present at the 7-position of the benzo ring of the structure of formula (I).

76. A compound of claim 60 wherein said one or more R^x are independently selected from the group consisting of $-OR^{13}$ and $-NR^{13}R^{14}$, wherein R^{13} and R^{14} are as defined in claim 2..

77. A compound of claim 76 wherein R^{13} and R^{14} are each methyl.

78. A compound of claim 60 wherein an R^y substituent is independently attached at the 3- or the 4-position of the phenyl ring of formula (II).

79. A compound of claim 60 wherein t is 1 or 2.

80. A compound of claim 60 wherein t is 1.

81. A compound of claim 60 wherein said one or more R^y are independently selected from the group consisting of hydrogen; halogen; hydroxy; $-NO_2$; $(C_1$-$C_{10})$alkyl; halo$(C_1$-$C_{10})$alkyl; aryl$(C_1$-$C_{10})$alkyl; heterocyclyl$(C_1$-$C_{10})$alkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; and $-NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^wA^-$; and -$CONR^9R^{10}$; and

wherein R^9, R^{10}, and R^w are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation.

82. A compound of claim 60 wherein said R^y is independently selected from the group consisting of hydrogen, chloro, fluoro, bromo, iodo, hydroxy, methoxy, ethoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, trimethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, trimethylammoniumethylcarbonylamino,

triethylammoniumethylcarbonylamino, trimethylammoniumpropylcarbonylamino, triethylammoniumpropylcarbonylamino, trimethylammoniumbutylcarbonylamino, triethylammoniumbutylcarbonylamino, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino, chloroethylcarbonylamino, fluoroethylcarbonylamino, bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino, chloropropylcarbonylamino, fluoropropylcarbonylamino, bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino, chlorobutylcarbonylamino, fluorobutylcarbonylamino, bromobutylcarbonylamino, iodobutylcarbonylamino, methoxycarbonyl, ethoxycarbonyl, trimethylammoniumethoxyethoxyethoxy, triethylammoniumethoxyethoxyethoxy, chloroethoxyethoxyethoxy, fluoroethoxyethoxyethoxy, bromoethoxyethoxyethoxy, iodoethoxyethoxyethoxy, pyridiniumethoxyethoxyethoxy, piperazinyloxymethoxyethoxyethoxy, methylpiperazinyloxymethoxyethoxyethoxy, dimethylpiperazinyloxymethoxyethoxyethoxy, piperidinyloxymethoxyethoxyethoxy, methylpiperidinyloxymethoxyethoxyethoxy, and dimethylpiperidinyloxymethoxyethoxyethoxyphenyl.

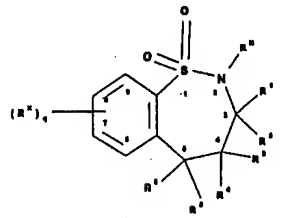
83. A compound of claim 60 wherein said one or more R^y are independently selected from the group consisting of hydroxy, methoxy, ethoxy, nitro, amino, methylamino, dimethylamino, ethylamino, diethylamino, trimethylammonium, triethylammonium, trimethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, trimethylammoniumethylcarbonylamino, triethylammoniumethylcarbonylamino, trimethylammoniumpropylcarbonylamino, triethylammoniumpropylcarbonylamino, trimethylammoniumbutylcarbonylamino,

triethylammoniumbutylcarbonylamino, methylcarbonylamino, chloromethylcarbonylamino, fluoromethylcarbonylamino, bromomethylcarbonylamino, iodomethylcarbonylamino, ethylcarbonylamino, chloroethylcarbonylamino, fluoroethylcarbonylamino, bromoethylcarbonylamino, iodoethylcarbonylamino, propylcarbonylamino, chloropropylcarbonylamino, fluoropropylcarbonylamino, bromopropylcarbonylamino, iodopropylcarbonylamino, butylcarbonylamino, chlorobutylcarbonylamino, fluorobutylcarbonylamino, bromobutylcarbonylamino, iodobutylcarbonylamino, trimethylammoniumethoxyethoxyethoxy, triethylammoniumethoxyethoxyethoxy, chloroethoxyethoxyethoxy, fluoroethoxyethoxyethoxy, bromoethoxyethoxyethoxy, iodoethoxyethoxyethoxy, and pyridiniumethoxyethoxyethoxy.

84. A compound of claim 60 wherein said one or more R^y are independently selected from the group consisting of trimethylammonium, triethylammonium, trimethylammoniummethylcarbonylamino, triethylammoniummethylcarbonylamino, trimethylammoniumethylcarbonylamino, triethylammoniumethylcarbonylamino, trimethylammoniumpropylcarbonylamino, triethylammoniumpropylcarbonylamino, trimethylammoniumbutylcarbonylamino, triethylammoniumbutylcarbonylamino, trimethylammoniumethoxyethoxyethoxy, and triethylammoniumethoxyethoxyethoxy.

85. A compound of claim 60 wherein said hydroxy group is in a *syn* relationship to said structure of formula (II).

86. A compound of formula (I):



(I)

wherein:

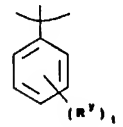
q is 1 or 2;

R^1 and R^2 are each independently alkyl;

R^3 is hydroxy;

R^4 and R^6 are hydrogen;

R^5 has the formula (II):



wherein t is an integer from 0 to 5;

one or more R^y are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y radicals optionally may have one or more carbons replaced by -O-; $-NR^7-$; $-N^+R^7R^8A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^7A^-$; $-PR^7-$; $-P(O)R^7-$; $-P^+R^7R^8A^-$; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl;

hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$; $-PR^9-$; $-P^+R^9R^{10}A^-$; $-P(O)R^9-$; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as defined in claim 2; and

R^N is selected from the group consisting of hydrogen; alkyl; and aralkyl; and

one or more R^x radicals are independently selected from the group consisting of alkoxy, alkylamino and dialkylamino; or

a pharmaceutically acceptable salt, solvate, or prodrug thereof.

87. A compound of claim 86 wherein R^1 and R^2 are each the same (C_1-C_{10})alkyl.

88. A compound of claim 86 wherein R^1 and R^2 are each n-butyl.

89. A compound of claim 86 wherein one or more R^x are independently selected from the group consisting of methoxy and dimethylamino.

90. A compound of claim 86 wherein q is 1.

91. A compound of claim 86 wherein q is 1, and R^x is selected from the group consisting of methoxy and dimethylamino.

92. A compound of claim 86 wherein R^N is selected from thegroup consisting of hydrogen; methyl, ethyl and benzyl.

93. A compound of claim 86 wherein said hydroxy group is in a *syn* relationship to said structure of formula (II).

94. A compound of claim 86 wherein t is 1.

95. A compound of claim 86 wherein t is 1 and R^y is in the para position.

96. A compound of claim 86 wherein t is 1 and R^y is in the meta position.

97. A compound of claim 86 wherein one or more R^y are independently selected from selected from the group consisting of halogen; hydroxy; -NO_2; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; and -$NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^WA^-$; and -$CONR^9R^{10}$; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation.

98. A compound of claim 97 wherein:
R^1 and R^2 are each the same (C_1-C_{10})alkyl;
one or more R^x are independently selected from the group consisting of methoxy and dimethylamino;
said hydroxy group is in a *syn* relationship to said structure of formula (II);
t is 1; and
R^y is in the meta or para position.

99. A compound of claim 97 wherein R^1 and R^2 are each n-butyl.

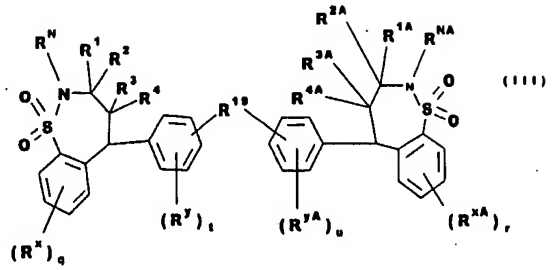
100. A compound of claim 97 wherein q is 1.

101. A compound of claim 97 wherein R^N is selected from the group consisting of hydrogen; methyl, ethyl and benzyl.

102. A compound of claim 97 wherein R^y is in the para position.

103. A compound of claim 97 wherein R^y is in the meta position.

104. A compound of the formula (III):



(III)

wherein :

q and r are independently integers from 0 to 4;

t and u are independently integers from 0 to 4;

R^1, R^2, R^{1A}, and R^{2A} are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl; or

R^{1A} and R^{2A} taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl;

wherein the R^1, R^2, R^{1A}, and R^{2A} alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^WA^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; -

PR^9R^{10}; $-P^+R^9R^{10}R^WA^-$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1, R^2, R^{1A}, and R^{2A} alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9-$; $-P(O)R^9-$; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; carboxyalkylamino; alkoxyalkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3, R^4, R^{3A}, and R^{4A} are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$; or

R^{3A} and R^{4A} together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cyanoalkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

one or more R^Y and R^{YA} are independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; -

SR^{13}; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y and R^{yA} radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y and R^{yA} radicals optionally may have one or more carbons replaced by -O-; $-NR^7$-; $-N^+R^7R^8A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$-; $-PR^7$-; $-P(O)R^7$-; $-P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A$-; $-S^+R^9R^{10}A$-; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9$-; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P^+R^9R^{10}A^-$-; $-P(O)R^9$-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein n is 0, 1 or 2; and

wherein M is a pharmaceutically acceptable cation; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as defined above; and

R^N and R^{NA} are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aralkyl; and heterocyclylalkyl; and

one or more R^X and R^{XA} radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; uaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-S(O)_2R^{13}$; $-SO_3R^{13}$; $-S^+R^{13}R^{14}A$-; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-NR^{14}C(O)R^{13}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-OR^{18}$; $-SO_nNR^{13}R^{18}$; -

$NR^{18}OR^{14}$; $-N^+R^{13}R^{14}R^{15}A^-$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue;

wherein the R^X and R^{XA} alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{11}R^{12}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^X and R^{XA} quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; $-N^+R^{13}R^{14}R^{15}A^-$; and carbohydrate residue; and

wherein the R^X and R^{XA} radicals comprising carbon optionally may have one or more carbons replaced by -O-; $-NR^{13}$-; $-N^+R^{13}R^{14}A^-$; -S-; -SO-; $-SO_2$-; $-S^+R^{13}A^-$-; $-PR^{13}$-; $-P(O)R^{13}$-; $-P^+R^{13}R^{14}A^-$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; $-NR^9$-; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9$-; $-P^+R^9R^{10}A^-$-; or $-P(O)R^9$-; and

wherein R^{18} is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R^{18} alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of

halogen; -CN ; NO_2; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{11}R^{12}A^-$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; $-CONR^9R^{10}$; $-SO_2OM$; $-SO_2NR^9R^{10}$; $-PR^9R^{10}$; $-P(OR^{16})OR^{17}$; $-PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^w, A^-, and M are as defined above; and

R^{19} is selected from the group consisting of alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate; amino acid; and peptide; polypeptide; wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polypeptide residue; can optionally have one or more carbons replaced by -O-; $-NR^7$-; $-N^+R^7R^8A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$-; $-PR^7$-; $-P^+R^7R^8A^-$-; phenylene; heterocyclyl; quaternary heterocyclyl; or aryl;

wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polypeptide residue can be substituted with one or more substituent groups independently selected from the group consisting of alkyl; alkenyl; alkynyl; polyalkyl; polyether; aryl; haloalkyl; cycloalkyl; heterocyclyl; arylalkyl; halogen; oxo; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-NO_2$; $-CO_2R^{13}$; -CN; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$;

wherein R^7, R^8, R^{11}, R^{12}, R^{13}, R^{14} R^{15}, and A^- are as defined above; or a pharmaceutically acceptable salt, solvate, or prodrug thereof.

105. A compound of claim 104 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of hydrogen and alkyl.

106. A compound of claim 104 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of hydrogen and C_1-C_{10} alkyl.

107. A compound of claim 104 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of C_2-C_7 alkyl.

108. A compound of claim 104 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of C_2-C_4 alkyl.

109. A compound of claim 104 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of ethyl; n-propyl; n-butyl; and isobutyl.

110. A compound of claim 104 wherein R^3, R^{3A}, R^4, and R^{4A} are independently selected from the group consisting of hydrogen and -OR^9, wherein R^9 is as defined in claim 104.

111. A compound of claim 110 wherein R^9 is hydrogen.

112. A compound of claim 104 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, alkyl and aralkyl.

113. A compound of claim 104 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl and aryl(C_1-C_{10})alkyl.

114. A compound of claim 104 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, methyl, ethyl and benzyl.

115. A compound of claim 104 wherein one or more R^x and R^{xA} are independently selected from the group consisting of methoxy and dimethylamino.

116. A compound of claim 104 wherein q and r are each 1.

117. A compound of claim 104 wherein one or more R^y are independently selected from selected from the group consisting of halogen; hydroxy; -NO_2; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl;

heterocyclyl(C_1-C_{10})alkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; and -$NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^WA^-$; and -$CONR^9R^{10}$; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

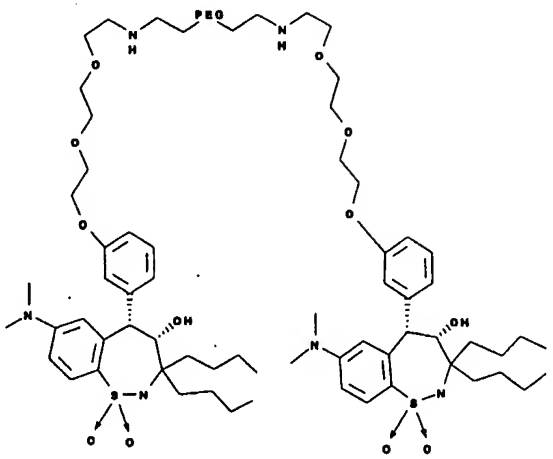
wherein M is a pharmaceutically acceptable cation.

118. A compound of claim 104 wherein R^{19} is selected from the group consisting of alkane diyl; polyalkane diyl; alkoxy diyl; and polyalkoxy diyl; wherein alkane diyl and polyalkane diyl can optionally have one or more carbons replaced by -O-; -NR^7-; -$N^+R^7R^8A^-$-; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -

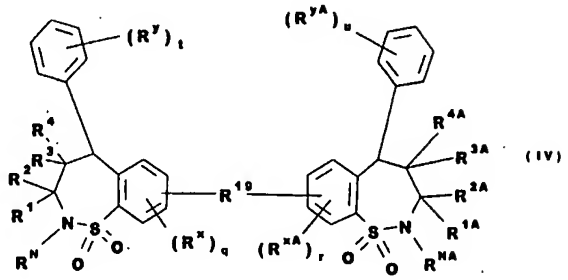
PR^7-; -P(O)R^7-; -$P^+R^7R^8A^-$-; or phenylene, wherein R^7 and R^8 are defined as in claim 104.

119. A compound of claim 104 wherein R^{19} is selected from the group consisting of alkoxy diyl and polyalkoxydiyl wherein one or more carbons are optionally replaced by -O-; -NR^7-; -$N^+R^7R^8A^-$-; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -PR^7-; -P(O)R^7-; -$P^+R^7R^8A^-$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; or polyalkyl, wherein R^9 and R^{10} are defined as in claim 104.

120. A compound of claim 104 having the formula:



121. A compound of the formula (IV):



wherein :

q and r are independently integers from 0 to 3;

t and u are independently integers from 0 to 5;

R^1, R^2, R^{1A}, and R^{2A} are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl; or

R^{1A} and R^{2A} taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl;

wherein the R^1, R^2, R^{1A}, and R^{2A} alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; -OR^9; -NR^9R^{10}; -$N^+R^9R^{10}R^wA^-$; -SR^9; -$S^+R^9R^{10}A^-$; -PR^9R^{10}; -$P^+R^9R^{10}R^wA^-$; -S(O)R^9; -SO_2R^9; -SO_3R^9; -CO_2R^9; and -$CONR^9R^{10}$; and

wherein the R^1, R^2, R^{1A}, and R^{2A} alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9-$; $-P(O)R^9-$; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; carboxyalkylamino; alkoxyalkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3, R^4, R^{3A}, and R^{4A} are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

R^{3A} and R^{4A} together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cyanoalkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

one or more R^y and R^{yA} are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-NR^{13}C(O)R^{14}$; $-NR^{13}C(O)NR^{14}R^{15}$; $-NR^{13}CO_2R^{14}$; $-OC(O)R^{13}$; $-OC(O)NR^{13}R^{14}$; $-NR^{13}SOR^{14}$; $-NR^{13}SO_2R^{14}$; $-NR^{13}SONR^{14}R^{15}$; $-NR^{13}SO_2NR^{14}R^{15}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y and R^{yA} radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; $-OR^7$; $-NR^7R^8$; $-SR^7$; $-S(O)R^7$; $-SO_2R^7$; $-SO_3R^7$; $-CO_2R^7$; $-CONR^7R^8$; $-N^+R^7R^8R^9A^-$; $-P(O)R^7R^8$; $-PR^7R^8$; $-P^+R^7R^8R^9A^-$; and $-P(O)(OR^7)OR^8$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y and R^{yA} radicals optionally may have one or more carbons replaced by -O-; $-NR^7-$; $-N^+R^7R^8A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$-; $-PR^7-$; $-P(O)R^7-$; $-P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl;

heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{11}R^{12}A^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{10}R^{11}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$; $-PR^9-$; $-P^+R^9R^{10}A^-$; $-P(O)R^9-$; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein n is 0, 1 or 2; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^w, and A^- are as defined above; and

R^N and R^{NA} are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aralkyl; and heterocyclylalkyl; and

one or more R^X and R^{XA} radicals are independently selected from the group consisting of hydrogen; halogen; -CN; $-NO_2$; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-S(O)_2R^{13}$; $-SO_3R^{13}$; $-S^+R^{13}R^{14}A^-$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-NR^{14}C(O)R^{13}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-OR^{18}$; $-SO_nNR^{13}R^{14}$; $-NR^{18}OR^{14}$; $-N^+R^{13}R^{14}R^{15}A^-$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue;

wherein the R^X and R^{XA} alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{11}R^{12}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^X and R^{XA} quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; $-N^+R^{13}R^{14}R^{15}A^-$; and carbohydrate residue; and

wherein the R^X and R^{XA} radicals comprising carbon optionally may have one or more carbons replaced by -O-; $-NR^{13}-$; $-N^+R^{13}R^{14}A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^{13}A^-$; $-PR^{13}-$; $-P(O)R^{13}-$; $-P^+R^{13}R^{14}A^-$; phenylene; amino acid; peptide; polypeptide; carbohydrate; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^9A^-$; $-PR^9-$; $-P^+R^9R^{10}A^-$; or $-P(O)R^9-$; and

wherein R^{18} is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R^{18} alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN ; NO_2; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{11}R^{12}A^-$; $-SR^9$; $-S(O)R^9$;

$-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; $-CONR^9R^{10}$; $-SO_2OM$; $-SO_2NR^9R^{10}$; $-PR^9R^{10}$; $-P(OR^{16})OR^{17}$; $-PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^v, A^-, and M are as defined above; and

R^{19} is selected from the group consisting of alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate; amino acid; and peptide; polypeptide; wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polypeptide residue; can optionally have one or more carbons replaced by -O-; $-NR^7-$; $-N^+R^7R^8A^-$; -S-; -SO-; $-SO_2-$; $-S^+R^7A^-$; $-PR^7-$; $-P(O)R^7-$; $-P^+R^7R^8A^-$; phenylene; heterocyclyl; quaternary heterocyclyl; or aryl;

wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polypeptide residue can be substituted with one or more substituent groups independently selected from the group consisting of alkyl; alkenyl; alkynyl; polyalkyl; polyether; aryl; haloalkyl; cycloalkyl; heterocyclyl; arylalkyl; halogen; oxo; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-NO_2$; $-CO_2R^{13}$; -CN; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; $-C(O)OM$; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^9R^{11}R^{12}A^-$;

wherein R^7, R^8, R^{11}, R^{12}, R^{13}, R^{14} R^{15}, and A^- are as defined above; or a pharmaceutically acceptable salt, solvate, or prodrug thereof.

122. A compound of claim 121 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of hydrogen and alkyl.

123. A compound of claim 121 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of hydrogen and C_1-C_{10} alkyl.

124. A compound of claim 121 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of C_2-C_7 alkyl.

125. A compound of claim 121 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of C_2-C_4 alkyl.

126. A compound of claim 121 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of ethyl; n-propyl; n-butyl; and isobutyl.

127. A compound of claim 121 wherein R^3, R^{3A}, R^4, and R^{4A} are independently selected from the group consisting of hydrogen and $-OR^9$, wherein R^9 is as defined in claim 121.

128. A compound of claim 126 wherein R^9 is hydrogen.

129. A compound of claim 121 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, alkyl and aralkyl.

130. A compound of claim 121 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl and aryl(C_1-C_{10})alkyl.

131. A compound of claim 121 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, methyl, ethyl and benzyl.

132. A compound of claim 121 wherein one or more R^x and R^{xA} are independently selected from the group consisting of methoxy and dimethylamino.

133. A compound of claim 121 wherein q and r are each 1.

134. A compound of claim 121 wherein one or more R^y are independently selected from selected from the group consisting of halogen; hydroxy; $-NO_2$; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl;

heterocyclyl(C_1-C_{10})alkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; and -$NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; haloC_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^wA^-$; and -$CONR^9R^{10}$; and

wherein R^9, R^{10} and R^w are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring;

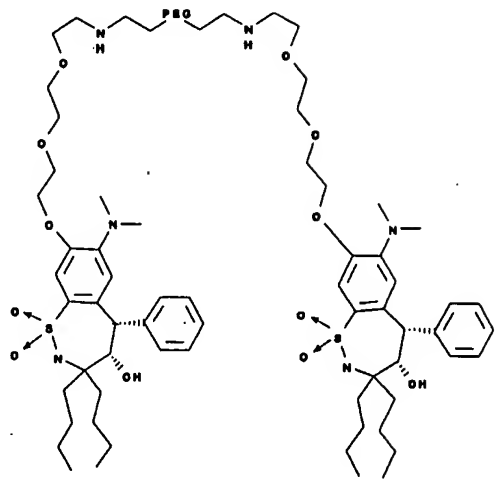
wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation.

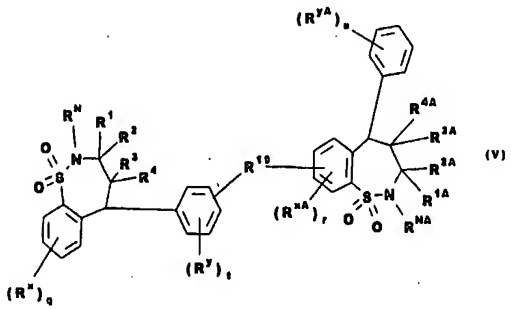
135. A compound of claim 121 wherein R^{19} is selected from the group consisting of alkane diyl; polyalkane diyl; alkoxy diyl; and polyalkoxy diyl; wherein alkane diyl and polyalkane diyl can optionally have one or more carbons replaced by -O-; -NR^7-; -$N^+R^7R^8A^-$-; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -PR^7-; -P(O)R^7-; -$P^+R^7R^8A^-$-; or phenylene, wherein R^7 and R^8 are defined as in claim 121.

136. A compound of claim 121 wherein R^{19} is selected from the group consisting of alkoxy diyl and polyalkoxydiyl wherein one or more carbons are optionally replaced by -O-; -NR^7-; -$N^+R^7R^8A^-$-; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -PR^7-; -P(O)R^7-; -$P^+R^7R^8A^-$-; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; or polyalkyl, wherein R^9 and R^{10} are defined as in claim 121.

137. A compound of claim 121 having the structural formula:



138. A compound of formula (V):



(V)

wherein :

q is an integer from 0 to 4;

r is an integer from 0 to 3;

t is an integer from 0 to 4;

u is an integer from 0 to 5;

R^1, R^2, R^{1A}, and R^{2A} are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl; or

R^1 and R^2 taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl; or

R^{1A} and R^{2A} taken together with the carbon to which they are attached form C_3-C_{10} cycloalkyl or C_3-C_{10} cycloalkenyl;

wherein the R^1, R^2, R^{1A}, and R^{2A} alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may be substituted with one or more radicals selected from the group consisting of -CN; halogen; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^9$; $-S^+R^9R^{10}A^-$; -

$P^+R^9R^{10}R^wA^-$; $-PR^9R^{10}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; and

wherein the R^1, R^2, R^{1A}, and R^{2A} alkyl; cycloalkyl; alkenyl; cycloalkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; alkoxyalkyl; alkoxyalkenyl; alkoxyalkynyl; aryloxyalkyl; aryloxyalkenyl; aryloxyalkynyl; heterocylcyloxyalkyl; heterocycloxyalkenyl; heterocyclyloxyalkynyl; alkylaryl; and (polyalkyl)aryl radicals optionally may have one or more carbons replaced by -O-; $-NR^9-$; $-N^+R^9R^{10}A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$-; $-PR^9-$; $-P(O)R^9-$; $-P^+R^9R^{10}A^-$-; or phenylene; and

wherein R^9, R^{10}, and R^W are independently selected from the group consisting of hydrogen; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; alkylammoniumalkyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; carboxyaryl; carboxyheterocyclyl; amino; alkylamino; carboxyalkylamino; alkoxyalkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

R^3, R^4, R^{3A}, and R^{4A} are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; and $-SO_3R^9$; or

R^3 and R^4 together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

R^{3A} and R^{4A} together form =O; $=NOR^9$; =S; $=NNR^9R^{10}$; $=NR^9$; or $=CR^{11}R^{12}$;

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; -CN; halogen; oxo; alkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; carboxyalkyl; alkoxyalkyl; carboalkoxyalkyl; cycloalkyl; cycloalkenyl; haloalkyl; hydroxyalkyl; cyanoalkyl; $-OR^9$; $-NR^9R^{10}$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; and $-CONR^9R^{10}$; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring; and

wherein R^9 and R^{10} are as defined above; and

one or more R^y and R^{yA} are independently selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; polyalkyl; haloalkyl; hydroxyalkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; -

SR^{13}; -S(O)R^{13}; -SO_2R^{13}; -SO_3R^{13}; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -C(O)$NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -$NR^{13}C(O)R^{14}$; -$NR^{13}C(O)NR^{14}R^{15}$; -$NR^{13}CO_2R^{14}$; -$OC(O)R^{13}$; -$OC(O)NR^{13}R^{14}$; -$NR^{13}SOR^{14}$; -$NR^{13}SO_2R^{14}$; -$NR^{13}SONR^{14}R^{15}$; -$NR^{13}SO_2NR^{14}R^{15}$; -P(O)$R^{13}R^{14}$; -$PR^{13}R^{14}$; -$P^+R^{13}R^{14}R^{15}A^-$; -$P(OR^{13})OR^{14}$; -$S^+R^{13}R^{14}A^-$; and -$N^+R^{13}R^{14}R^{15}A^-$; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y and R^{yA} radicals optionally may be further substituted with one or more radicals selected from the group consisting of -CN; halogen; hydroxy; oxo; alkyl; cycloalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclyl; -OR^7; -NR^7R^8; -SR^7; -S(O)R^7; -SO_2R^7; -SO_3R^7; -CO_2R^7; -$CONR^7R^8$; -$N^+R^7R^8R^9A$-; -P(O)R^7R^8; -PR^7R^8; -$P^+R^7R^8R^9A^-$; and -P(O)(OR^7)OR^8; and

wherein the alkyl, polyalkyl, haloalkyl, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, quaternary heterocyclyl, arylalkyl, heterocyclylalkyl, and polyether substituents of the R^y and R^{yA} radicals optionally may have one or more carbons replaced by -O-; -NR^7-; -$N^+R^7R^8A$--; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -PR^7-; -P(O)R^7-; -$P^+R^7R^8A^-$-; or phenylene; and

wherein R^7 and R^8 are independently selected from the group consisting of hydrogen; alkyl, alkenyl; alkynyl; aryl; and heterocyclyl; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether; or

wherein R^{13} and R^{14} together with the nitrogen atom to which they are attached form a mono- or polycyclic heterocyclyl that is optionally substituted with one or more radicals selected from the group consisting of oxo, carboxy, and quaternary salts; or

wherein R^{14} and R^{15} together with the nitrogen atom to which they are attached form a cyclic ring; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; sulfo; oxo; alkyl; haloalkyl; hydroxyalkyl; sulfoalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclylalkyl; carboxy; carboxyalkyl; guanidinyl; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{11}R^{12}A^-$; -SR^{16}; -S(O)R^9; -SO_2R^9; -SO_3R^{16}; -CO_2R^{16}; -$CONR^9R^{10}$; -$SO_2NR^9R^{10}$; -$PO(OR^{16})OR^{17}$; -PR^9R^{10}; -$P^+R^9R^{10}R^{11}A$-; -$S^+R^9R^{10}A$-; and carbohydrate residue; and

wherein the R^{13}, R^{14}, and R^{15} alkyl; haloalkyl; cycloalkyl; polyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; quaternary heterocyclylalkyl; alkylarylalkyl; alkylheterocyclylalkyl; alkylammoniumalkyl; aminocarbonylalkyl; alkylaminocarbonylalkyl; carboxyalkylaminocarbonylalkyl; and polyether radicals optionally may have one or more carbons replaced by -O-; -NR^9-; -$N^+R^9R^{10}A$-; -S-; -SO-; -SO_2-; -$S^+R^9A^-$-; -PR^9-; -$P^+R^9R^{10}A^-$-; -P(O)R^9-; phenylene; carbohydrate residue; amino acid residue; peptide residue; or polypeptide residue; and

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

wherein M is a pharmaceutically acceptable cation; and

wherein n is 0, 1 or 2; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^W and A^- are as defined above; and

R^N and R^{NA} are independently selected from the group consisting of hydrogen; alkyl; alkenyl; alkynyl; aralkyl; and heterocyclylalkyl; and

one or more R^X and R^{XA} radicals are independently selected from the group consisting of hydrogen; halogen; -CN; -NO_2; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy; -OR^{13}; -$NR^{13}R^{14}$; -SR^{13}; -S(O)R^{13}; -$S(O)_2R^{13}$; -SO_3R^{13}; -$S^+R^{13}R^{14}A$-; -$NR^{13}OR^{14}$; -$NR^{13}NR^{14}R^{15}$; -CO_2R^{13}; -OM; -SO_2OM; -$SO_2NR^{13}R^{14}$; -$NR^{14}C(O)R^{13}$; -C(O)$NR^{13}R^{14}$; -C(O)OM; -COR^{13}; -OR^{18}; -$S(O)_nNR^{13}R^{14}$;

$-NR^{13}R^{18}$; $-NR^{18}OR^{14}$; $-N^+R^{13}R^{14}R^{15}A^-$; $-PR^{13}R^{14}$; $-P(O)R^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; amino acid residue; peptide residue; polypeptide residue; and carbohydrate residue;

wherein the R^X and R^{XA} alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; acyloxy radicals optionally may be further substituted with one or more radicals selected from the group consisting of halogen; -CN; oxo; $-OR^{16}$; $-NR^9R^{10}$; $-N^+R^9R^{10}R^wA^-$; $-SR^{16}$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^{16}$; $-CO_2R^{16}$; $-CONR^9R^{10}$; $-SO_2NR^9R^{10}$; $-PO(OR^{16})OR^{17}$; $-PR^9R^{10}$; $-P^+R^9R^{11}R^{12}A^-$; $-S^+R^9R^{10}A^-$; and carbohydrate residue; and

wherein the R^X and R^{XA} quaternary heterocyclyl radical optionally may be substituted with one or more radicals selected from the group consisting of halogen; -CN; $-NO_2$; oxo; alkyl; cycloalkyl; polyalkyl; haloalkyl; hydroxyalkyl; alkenyl; alkynyl; aryl; heterocyclyl; arylalkyl; heterocyclylalkyl; polyether; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-CO_2R^{13}$; OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; $-N^+R^{13}R^{14}R^{15}A^-$; and carbohydrate residue; and

wherein the R^X and R^{XA} radicals comprising carbon optionally may have one or more carbons replaced by -O-; $-NR^{13}$-; $-N^+R^{13}R^{14}A^-$; -S-; -SO-; $-SO_2$-; $-S^+R^{13}A^-$; $-PR^{13}$-; $-P(O)R^{13}$-; $-P^+R^{13}R^{14}A^-$; phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; polyether; or polyalkyl; wherein said phenylene; amino acid residue; peptide residue; polypeptide residue; carbohydrate residue; and polyalkyl optionally may have one or more carbons replaced by -O-; $-NR^9$-; $-N^+R^9R^{10}A^-$; -S-; -SO-; $-SO_2$-; $-S^+R^9A^-$; $-PR^9$-; $-P^+R^9R^{10}A^-$; or $-P(O)R^9$-; and

wherein R^{18} is selected from the group consisting of alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl; and

wherein the R^{18} alkyl; alkenyl; alkynyl; aryl; heterocyclyl; quaternary heterocyclyl; arylalkyl; heterocyclylalkyl; acyl; alkoxycarbonyl; arylalkoxycarbonyl; and heterocyclylalkoxycarbonyl radicals optionally may be substituted with one or more radicals selected from the group consisting of

halogen; -CN ; NO_2; oxo; $-OR^9$; $-NR^9R^{10}$; $-N^+R^9R^{11}R^{12}A^-$; $-SR^9$; $-S(O)R^9$; $-SO_2R^9$; $-SO_3R^9$; $-CO_2R^9$; $-CONR^9R^{10}$; $-SO_2OM$; $-SO_2NR^9R^{10}$; $-PR^9R^{10}$; $-P(OR^{16})OR^{17}$; $-PO(OR^{16})OR^{17}$; and -C(O)OM; and

wherein R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^w, A^-, and M are as defined above; and

R^{19} is selected from the group consisting of alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polypeptide residue; wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide residue; and polypeptide residue; can optionally have one or more carbons replaced by -O-; $-NR^7$-; $-N^+R^7R^8A^-$-; -S-; -SO-; $-SO_2$-; $-S^+R^7A^-$-; $-PR^7$-; $-P(O)R^7$-; $-P^+R^7R^8A^-$-; phenylene; heterocyclyl; quaternary heterocyclyl; or aryl;

wherein alkane diyl; alkene diyl; alkyne diyl; polyalkane diyl; alkoxy diyl; polyether diyl; polyalkoxy diyl; carbohydrate residue; amino acid residue; peptide; and polypeptide residue can be substituted with one or more substituent groups independently selected from the group consisting of alkyl; alkenyl; alkynyl; polyalkyl; polyether; aryl; haloalkyl; cycloalkyl; heterocyclyl; arylalkyl; halogen; oxo; $-OR^{13}$; $-NR^{13}R^{14}$; $-SR^{13}$; $-S(O)R^{13}$; $-SO_2R^{13}$; $-SO_3R^{13}$; $-NR^{13}OR^{14}$; $-NR^{13}NR^{14}R^{15}$; $-NO_2$; $-CO_2R^{13}$; -CN; -OM; $-SO_2OM$; $-SO_2NR^{13}R^{14}$; $-C(O)NR^{13}R^{14}$; -C(O)OM; $-COR^{13}$; $-P(O)R^{13}R^{14}$; $-PR^{13}R^{14}$; $-P^+R^{13}R^{14}R^{15}A^-$; $-P(OR^{13})OR^{14}$; $-S^+R^{13}R^{14}A^-$; and $-N^+R^{13}R^{14}R^{15}A^-$;

wherein R^7, R^8, R^{11}, R^{12}, R^{13}, R^{14} R^{15}, and A^- are as defined above; or a pharmaceutically acceptable salt, solvate, or prodrug thereof.

139. A compound of claim 138 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of hydrogen and alkyl.

140. A compound of claim 138 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of hydrogen and C_1-C_{10} alkyl.

141. A compound of claim 138 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of C_2-C_7 alkyl.

142. A compound of claim 138 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of C_2-C_4 alkyl.

143. A compound of claim 138 wherein R^1, R^{1A}, R^2, and R^{2A} are independently selected from the group consisting of ethyl; n-propyl; n-butyl; and isobutyl.

144. A compound of claim 138 wherein R^3, R^{3A}, R^4, and R^{4A} are independently selected from the group consisting of hydrogen and -OR^9, wherein R^9 is as defined in claim 138.

145. A compound of claim 144 wherein R^9 is hydrogen.

146. A compound of claim 138 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, alkyl and aralkyl.

147 A compound of claim 138 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, (C_1-C_{10})alkyl and aryl(C_1-C_{10})alkyl.

148. A compound of claim 138 wherein R^N and R^{NA} are independently selected from the group consisting of hydrogen, methyl, ethyl and benzyl.

149. A compound of claim 138 wherein one or more R^x and R^{xA} are independently selected from the group consisting of methoxy and dimethylamino.

150. A compound of claim 138 wherein q and r are each 1.

151. A compound of claim 138 wherein one or more R^y are independently selected from selected from the group consisting of halogen; hydroxy; -NO_2; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl;

heterocyclyl(C_1-C_{10})alkyl; polyether; -OR^{13}; -$NR^{13}R^{14}$; and -$NR^{13}C(O)R^{14}$; and

wherein R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether; or

wherein the R^{13}, R^{14}, and R^{15} (C_1-C_{10})alkyl;halo(C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; quaternary heterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylheterocyclyl(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; and polyether radicals optionally may be substituted with one or more radicals selected from the group consisting of halogen; (C_1-C_{10})alkyl; heterocyclyl; quaternary heterocyclyl; quaternary heterocyclyl(C_1-C_{10})alkyl; carboxy; carboxy(C_1-C_{10})alkyl; -OR^{16}; -NR^9R^{10}; -$N^+R^9R^{10}R^WA^-$; and -$CONR^9R^{10}$; and

wherein R^9 and R^{10} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; ammonium(C_1-C_{10})alkyl; (C_1-C_{10})alkylammonium(C_1-C_{10})alkyl; aryl(C_1-C_{10})alkyl; heterocyclyl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; carboxyheterocyclyl; carboxy(C_1-C_{10})alkylamino; and acyl; and

wherein A^- is a pharmaceutically acceptable anion; and

wherein R^{11} and R^{12} are independently selected from the group consisting of hydrogen; (C_1-C_{10})alkyl; heterocyclyl; aryl(C_1-C_{10})alkyl; carboxy(C_1-C_{10})alkyl; and carbo(C_1-C_{10})alkoxy(C_1-C_{10})alkyl; or

R^{11} and R^{12} together with the carbon atom to which they are attached form a cyclic ring;

wherein R^{16} and R^{17} are independently selected from the group consisting of R^9 and M; and

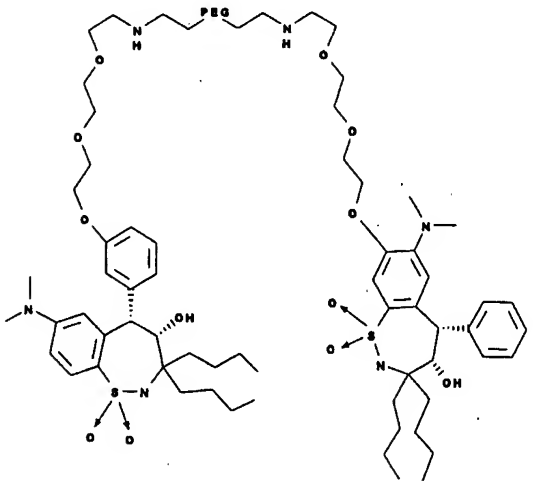
wherein M is a pharmaceutically acceptable cation.

152. A compound of claim 138 wherein R^{19} is selected from the group consisting of alkane diyl; polyalkane diyl; alkoxy diyl; and polyalkoxy diyl; wherein alkane diyl and polyalkane diyl can optionally have one or more carbons replaced by -O-; -NR^7-; -$N^+R^7R^8A^-$-; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -

PR^7-; -P(O)R^7-; -$P^+R^7R^8A^-$-; or phenylene, wherein R^7 and R^8 are defined as in claim 138.

153. A compound of claim 138 wherein R^{19} is selected from the group consisting of alkoxy diyl and polyalkoxydiyl wherein one or more carbons are optionally replaced by -O-; -NR^7-; -$N^+R^7R^8A^-$-; -S-; -SO-; -SO_2-; -$S^+R^7A^-$-; -PR^7-; -P(O)R^7-; -$P^+R^7R^8A^-$-; phenylene; amino acid; peptide; polypeptide; carbohydrate; or polyalkyl, wherein R^9 and R^{10} are defined as in claim 138.

154. A compound of claim 138 having the formula:



155. A pharmaceutical composition comprising an anti-hyperlipidemic effective amount of a compound of formula (I) of claim 1; and
a pharmaceutically acceptable carrier.

156. A pharmaceutical composition comprising an anti-atherosclerotic effective amount of a compound of formula (I) of claim 1; and
a pharmaceutically acceptable carrier.

157. A pharmaceutical composition comprising an anti-hypercholesterolemia effective amount of a compound of formula (I) of claim 1; and
a pharmaceutically acceptable carrier.

158. A pharmaceutical composition comprising an anti-hyperlipidemic effective amount of a compound of formula (I) of claim 2; and
a pharmaceutically acceptable carrier.

159. A pharmaceutical composition comprising an anti-atherosclerotic effective amount of a compound of formula (I) of claim 2; and
a pharmaceutically acceptable carrier.

160. A pharmaceutical composition comprising an anti-hypercholesterolemia effective amount of a compound of formula (I) of claim 2; and
a pharmaceutically acceptable carrier.

161. A method for the prophylaxis or treatment of a hyperlipidemic condition comprising administering to a patient in need thereof a composition of claim 155 in unit dosage form.

162 A method for the prophylaxis or treatment of an atherosclerotic condition comprising administering to a patient in need thereof a composition of claim 156 in unit dosage form.

163. A method for the prophylaxis or treatment of hypercholesterolemia comprising administering to a patient in need thereof a composition of claim 157 in unit dosage form.

164. A method for the prophylaxis or treatment of a hyperlipidemic condition comprising administering to a patient in need thereof a composition of claim 158 in unit dosage form.

165. A method for the prophylaxis or treatment of an atherosclerotic condition comprising administering to a patient in need thereof a composition of claim 159 in unit dosage form.

166. A method for the prophylaxis or treatment of hypercholesterolemia comprising administering to a patient in need thereof a composition of claim 160 in unit dosage form.

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(71) Applicant *(for all designated States except US)*: G.D. SEARLE & CO. [US/US]; Corporate Patent Department, 5200 Old Orchard Road, Skokie, IL 60077 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: TOLLEFSON, Michael, B. [US/US]; 357 Big Horn Drive, Hainesville, IL 60030 (US). KOLODZIEJ, Steve, A. [US/US]; 2448 Clarjon Road, Ballwin, MO 63021 (US). REITZ, David, B. [US/US]; 14814 Pleasant Ridge Court, Chesterfield, MO 63017 (US).

(74) Agents: WARNER, James, M. et al.; G.D. Searle & Co., Corporate Patent Department, 5200 Old Orchard Road, Skokie, IL 60077 (US).

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(54) Title: 1,2-BENZOTHIAZEPINES FOR THE TREATMENT OF HYPERLIPIDEMIC DISEASES

(57) Abstract: Novel 1,1-dioxido-1,2-benzothiazepines, derivatives and analogs thereof, pharmaceutical compositions containing them, and their use in medicine, particularly in the prophylaxis and/or treatment of hyperlipidemic diseases, conditions and/or disorders, such as those associated with atherosclerosis and/or hypercholesterolemia.

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IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 38182 A (GLAXO GROUP LTD ;HANDLON ANTHONY LOUIS (US); HODGSON GORDON LEWIS) 3 September 1998 (1998-09-03) Formula (Ie) claims 1,6 ---	1-103
A	WO 98 02432 A (SUGIURA YOSHIHIRO ;DOI TAKAYUKI (JP); KATO KANEYOSHI (JP); KAWADA) 22 January 1998 (1998-01-22) cited in the application claim 8 ---	1
A	WO 96 16051 A (WELLCOME FOUND ;BRIEADDY LAWRENCE EDWARD (US); HANDLON ANTHONY LOU) 30 May 1996 (1996-05-30) cited in the application claim 1 ---	1-103

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 July 2000	09.08.00

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3018	Gettins, M

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/02503

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 05188 A (WELLCOME FOUND ;BRIEADDY LAWRENCE EDWARD (US)) 22 February 1996 (1996-02-22) cited in the application claim 1 ---	1-103

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/02503

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9838182 A	03-09-1998	AU 6823898 A	18-09-1998
WO 9802432 A	22-01-1998	AU 3460797 A	09-02-1998
		JP 10338672 A	22-12-1998
WO 9616051 A	30-05-1996	AT 189891 T	15-03-2000
		AU 706325 B	17-06-1999
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		BR 9509683 A	16-09-1997
		CZ 9701473 A	12-11-1997
		DE 69515183 D	30-03-2000
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WO 9605188 A	22-02-1996	AP 720 A	08-01-1999
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		SK 17797 A	10-09-1997

Form PCT/ISA/210 (patent family annex) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/02503

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 161-166 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 104-154 -all other claims only searched partially
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 104-154 -all other claims only searched partially

Present claims 1-166 relate to an extremely large number of possible compounds. In fact, the claims contain so many options, variables, possible permutations (e.g. prodrug) , huge definitions (such as hydrocarbyl or containing at least one heteroatom) and provisos that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely those compounds recited in the physically characterised and tested examples 1-24 on pages 284-327 and closely related homologous compounds as defined in the next paragraph. It is noted that only compounds of the formula (I) appear to have been exemplified and that there are no examples of formulae (III). (IV) or (V). It should be noted that only examples which are clearly defined and physically characterised have been taken into consideration. Examples 101-1652 do not appear to be be defined as regards the RN substituent and are therefore not examples which are adequately defined for supporting the scope of the claims.

The search has been limited to the examples and a generalisation thereof to compounds of formula (I) in which R3 and R4 are H and OH, R5 is hydrogen and R6 is a (substituted) phenyl.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.